AGEING 2016

ABSTRACTS

9th - 11th February 2016
London, UK

EuroSciCon

This annual international summit will look at many facets of research and processes that are involved in ageing and senescence. With discussions ranging from discovery of biomarkers and assay development to immunology, this event promises to be packed with discussion and debate and is an ideal opportunity to discover what is new in the field. With an all-round view of ageing, from diagnostics to therapy, this event will be multi-disciplinary.

This event has CPD accreditation

This is a draft abstract book
The abstract book will be finalised two weeks before the event
www.regonline.co.uk/ageing2016

#Ageing2016

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Invited Speakers Abstracts

Ageing, Autophagy and Neurodegenerative Disease

Professor Christian Behl, Chair and Director of the Institute of Pathobiochemistry, University Medical Center, Mainz, Germany

Ageing is the primary risk factor for various human neurodegenerative disorders and many interdependent factors and mechanisms influence the ageing of cells and organisms which can be integrated and summarized in a "molecular ageing matrix" theory of ageing. Of key importance for the function of ageing neurons is the maintenance of intracellular protein homeostasis. Protein accumulation can lead to neuronal dysfunction and an effective and controlled degradation via the proteasome and autophagy is essential for the clearance of dysfunctional proteins. During cellular ageing the lysosomal-autophagic decomposition of proteins rises, probably due to an increased demand; but degradation pathways can become impaired or overburdened. Factors that mediate the strictly controlled pathway of macroautophagy, in particular, need to be understood. Interestingly, some of the so far identified modifiers and regulators of macroautophagy carry out multiple functions in the cell, for instance RAB proteins involved in vesicle trafficking or the co-chaperone BAG3 known as prominent interactor of HSP70. The identification of such key regulators of selective macroautophagy will provide new approaches to stabilize neurons and keep them functional despite age-associated extra- and intracellular stress overall representing a novel way for the prevention of neurodegenerative disorders.

Chromosome Behaviour in Senecent Cells and in Hutchinson-Gilford Progeria Syndrome Cells

Dr Joanna M. Bridger BSc (Hons), MA, PhD, FSB, Reader of Chromosome Behaviour, Brunel University London, UK

We have found that specific chromosomes sit in different non-random locations within cell nuclei depending on whether a primary cell has become senescent or is still proliferating. This reproducible and specific positioning has the potential to be a biomarker for replicative senescence. Furthermore, in the premature ageing disease Hutchinson-Gilford Progeria Syndrome, a good model for normal ageing, chromosomes are mis-positioned and behave differently with respect to interactions with nuclear structure. We have been able to restore specific chromosome positions and dynamics through nuclear motors with specific drug treatments and not others.

A neural code for food abundance that modulates lifespan

Dr QueeLim Ch'ng, MRC Centre for Developmental Neurobiology, King's College London, UK

Food affects ageing via the nervous system. We discovered that gene expression in specific neurons encodes food abundance to modulate lifespan. TGFβ and tryptophan hydroxylase (which synthesizes serotonin) mediate food-dependent lifespan changes, and their expression are food-responsive. Crosstalk and auto-regulation between them alters the shape, dynamic range, and variance of their food responses. These regulatory features provide distinct mechanisms for TGFβ and serotonin to tune the accuracy of this neural code, which impacts the influence of food on lifespan. These multifaceted gene-environment interactions in conserved nutrient sensors provide a neural link from food to physiology.

Do microRNAs mediate sarcopenia development?

Dr Katarzyna Goljanek-Whysall, enure-Track Fellow, Musculoskeletal Biology II, Institute of Ageing and Chronic Disease University of Liverpool, UK

A common characteristic of ageing is loss of skeletal muscle (sarcopenia) leading to a decreased life quality. microRNAs are novel regulators of gene expression expression of which changes in muscle during ageing. We identified changes in microRNA expression in muscle and chose 2 microRNAs for further studies of their role in sarcopenia development. We microRNA expression in vivo, in adult and old mice, and established their role in muscle homeostasis. We demonstrated that dysregulation of expression of a single microRNA can affect myofibre size and force generation by muscle. This could lead to design of novel therapeutics against sarcopenia.

Developing age appropriate drug formulations for older patients

Dr Mine Orlu Gul, UCL School of Pharmacy, Department of Pharmaceutics, London, UK

The current patient-centric formulation development specifically for geriatric patients is limited. However, steps are taken to improve the present status. The European Medicines Agency`s Geriatric Medicines Strategy, FDA`s Guidance of Industry E7 Studies in Support of Special Populations: Geriatrics - Questions and Answers document and EFPIA Position Paper on Drug Development for Older and Ageing Patients are promising to increase the availability of medicines tailored for needs of older patients. The review of current scientific literature shows that further research should be performed to rationalize formulation development for elderly. Besides the conventional biopharmaceutical properties of the drug and quality aspects of the formulation, organoleptic properties such as ease of swallowing, taste and simplicity of opening packaging should be considered at early stage of product development due to the potential impact on patient acceptability. The presentation will cover several ongoing scientific studies to explore the pharmaceutical needs and solutions under the light of the opinion of older people obtained during public engagement workshops.

Splicing factors as determinants of longevity

Professor Lorna Harries, Peninsula College of Medicine and Dentistry, University of Exeter, Exeter, United Kingdom

Is Alzheimer's disease a disease or simply a manifestation of ageing?

Professor Emeritus Amos D Korczyn, Department of Neurology, Tel Aviv University, Ramat Aviv, Israel

Attempts to find cure for Alzheimer's disease (AD) have failed so far, in spite of enormous investments, intellectual and financial. It is unlikely that attacking a downstream phenomenon, like apoptosis or-amyloid, can cure AD, or prevent its progression.

Senile dementia is the result of a combination of several processes. Epidemiological studies have identified many risk factors, some genetic but most environmental and therefore modifiable. Therefore a concerted action to fight the dementia epidemic must be made by aggressive action against its risk factors, and this battle must begin in midlife, not in old age.

Aging starts Early, In Utero: A Trigger for Parturition

Dr Ramkumar Menon, Department of Obstetrics and Gynecology, Maternal-Fetal Medicine & Perinatal Research Division, The University of Texas Medical Branch, USA

Age related pathologies are associated with adult onset diseases like several cancers, diabetes, Alzheimer's, and cardiovascular risks but many of these diseases are programmed during in utero life. The new concept introduced in my lab is that aging starts early during in utero growth and development of the fetus. Signals of senescence generated by maturing fetal tissues can signal parturition. Similarly, premature aging can contribute to adverse pregnancy outcome and also program the fetus inadvertently for adult onset diseases. This lecture will discuss the role of senescence of fetal tissues as a mechanistic signals of fetal maturation process to initiate parturition.

Osteoarthritis handling the threat by finding a treatment

Dr Yolande FM Ramos, Dept. Medical Statistics and Bioinformatics, Section Molecular Epidemiology, Leiden University Medical Center, Leiden, The Netherlands

By performing genetic studies to symptomatic osteoarthritis patients, the group of Dr. Meulenbelt has identified the deiodinase iodothyronine type II (D2) gene (DIO2) as a robust OA susceptibility gene. Functional follow up studies show that age related loss of epigenetic control of the DIO2 gene with ongoing OA pathology affects the propensity of OA chondrocytes recuperate a growth plate morphology and exhibit debilitating expression. Focused functional follow-up of OA susceptibility genes to elucidate underlying pathophysiological mechanisms may contribute to a desirable translation from genetic studies towards novel therapeutic options.

Peculiarities of relations between cerebrovascular system, SCF-dynamics and Scull mechanical properties for aging persons.

Professor Yuri Moskalenko, D.Sci., Honor Scientist of RF, D.O.(Honoris Causa, Cn.).Sechenov Institute of evolutionary physiology and Biochemistry, Russian Academy of Sciences, Russian School of osteopathic medicine, Sankt Petersburg, Russian Federation

Instrumental investigations, using modern microelectronic units, coupling with computer techniques, have been shown, that the circulatory - metabolic support of brain functioning is generally based of integrative relations of brain circulatory system, CSF circulation, including ICF, which drainage brain tissue from wastes and mechanic properties of skull, which responsible for maintain liquid chemical-physical homeostasis inside crania-spinal cavity. That is why, aging decrease of cerebral blood flow is compensating by increase of CSF mobility and Cranial Compliance. One of real ways of preventing circulatory dementia may by based on additional increase of CSF-mobility in the crania-spinal spaces and correction of skull pattern by applications of techniques of osteopathic medicine. Supported by Grant RFFI 15-04-598.

Immunity and Ageing: causes and consequences of immunosenescencein humans

Professor Graham Pawelec, Second Department of Internal Medicine, University of Tübingen Medical School, Tübingen, Germany

The immune system defends against infection, but older people paradoxically suffer both from failing immunity resulting in increased susceptibility to infections and decreased responsiveness to vaccination, and at the same time increased immunopathology and inflammation accompanying immune responses. Interventions to reduce such deleterious effects while enhancing protective immunity need to be confronted if we are to deal successfully with the increasing numbers of elderly and frail people in modern societies. Defining relevant age-associated alterations and identifying reliable biomarkers for monitoring clinically-relevant immune status in the elderly is crucial to overcoming these problems, as will be discussed in this presentation.

The roll of genomic instability in vascular ageing

Dr Anton J.M. Roks, Dept. of Internal Medicine, Division of Vascular Disease and Pharmacology, Erasmus Medical Center, Erasmus University, Rotterdam, Netherlands

Genomic instability has been recognized as a primary contributor to the ageing process. Except for its relation to human accelerated ageing syndromes, it can be promoted in mouse models by genetically induced DNA repair dysfunction leading to similar ageing characteristic as observed in humans. In the present lecture we will discuss the contribution of genomic instability to vascular ageing as found in humans and mouse models. Further, we discuss the potential usefulness of the mouse models for clinical translation in the field of cardiovascular disease.

Genetic and epigenetic investigation of C9orf72: diagnostic implications for ALS and FTD

Dr Ekaterina Rogaeva, Associate Professor and Chair in Research on Dementia with Lewy Bodies, Centre for Research in Neurodegenerative Diseases, University of Toronto, Canada

An expanded repeat in C9orf72 is the most common genetic cause of both amyotrophic lateral sclerosis (ALS) and frontotemporal lobar dementia (FTD). However, the lower limit for pathological expansions is unknown. Recently we reported a family in whom a 70-repeat allele from the father expanded to ~2000 repeats during parent-offspring transmission leading to the first generation affected by ALS. Epigenetic and RNA analyses further discriminated the small and large expansions. Our findings support a hypothesis of multiple origins for the expansion and might help explain the unusually high frequency of sporadic ALS and FTD cases with expansion in C9orf72.

Identification and preclinical development of Salvia haenkeii extract as powerful anti-senescent agent using a novel screening method

Dr Giovanni Rizzo, iDNA Ltd/University College London, London, United Kingdom

The short-term activation of senescence inhibits tumour progression and induces would healing while long-term presence of senescent cells has the potential to promote age-related disease. Thus, the identification of pro- and anti-senescence molecules may lead to new therapeutic strategies for cancer and age-related diseases, respectively. By using a novel molecular screening platform that identifies anti-senescent compounds many extracts have identified with anti-ageing properties. Particularly, we

report for the first time that leaf extract of Salvia haenkeii can prevent replicative- and photo-ageing senescence. Moreover, we have shown that extract from Salvia haenkeii is safe for dermatological use suggesting it is a promising candidate for anti-ageing treatment.

Functional exhaustion of skeletal muscle stem cells during tissue aging

Alessandra Sacco, Associate Professor, Development, Aging andRegeneration Program, Sanford-Burnham-Prebys Medical Discovery Institute, La Jolla, USA

Age-related skeletal muscle decline is associated with functional impairment of muscle stem cells, tissue-resident stem cells required for tissue growth, maintenance and repair. The presentation will focus on emerging mechanisms, both intrinsic and extrinsic, driving this progressive dysregulation.

White and brown adipose tissue interplay: effect on weight and metabolic control during aging.

Dr Labros Sidossis, Shriners Hospitals for Children, University of Texas Medical Branch at Galveston, TX, USA

Since the presence of brown adipose tissue (BAT) was confirmed in adult humans, BAT has become a therapeutic target for obesity and insulin resistance. However, it soon became obvious that BAT dissapears as we age and there is less of it in obese individuals. In this lecture we will review the latest on BAT metabolism as we age and present exiting new data on browning of the white adipose tissue.

The epigenetic diet and its role in ageing

Dr Trygve Tollefsbol, University of Alabama at Birmingham, Birmingham, AL, USA

Key genes are controlled through epigenetic mechanisms and are influenced by dietary changes. We have found that dietary phytochemicals such as sulforaphane (SFN) and epigallocatechin-3-gallate (EGCG) inhibit telomerase gene (hTERT) activity through epigenetic mechanisms. Further, reduced glucose provided to normal human cells in vitro extends their lifespan and leads to cell death of precancerous cells. These studies indicate that a diet rich in phytochemicals may prevent cancer and that sugar reduction may slow aging and contribute to cancer prevention through epigenetic effects.

Is age 'written' in your blood?

Dr Athina Vidaki, Department of Pharmacy and Forensic Science, Faculty of Life Sciences and Medicine, King's College London, London, United Kingdom

Estimating an individual's biological age can be of great use in studying ageing or predicting disease susceptibility; however, estimating someone's chronological age would also be of a significant value in criminal investigations. In cases where there are no suspects or no eye-witnesses available to provide investigative leads, predicting a bloodstain donor's age could eliminate potential suspects. We have developed a DNA methylation-based next generation sequencing approach that simultaneously analyses a set of age-associated epigenetic markers; nevertheless, extensive validation is necessary to account for various medical or environmental factors.

Is loneliness really bad for old people?

Professor Christina R. Victor, Professor of Gerontology and public health, Brunel University London, UK

This talk will consider the prevalence of loneliness among older people; consider the key risk factors for loneliness and critically evaluate the evidence suggesting that there are negative health outcomes, such as mortality, dementia/cognitive impairment and increased health service use resultant from loneliness. We will consider if these outcomes are a cause or consequence of loneliness.

Biopsychosocial Effects of Aging with HIV: Implications for Research and Practice

Dr David E. Vance, School of Nursing, The University of Alabama at Birmingham, USA

By 2020, 70% of adults with HIV will be 50 and older. Although a testament to the effectiveness of combination antiretroviral therapy, aging with this disease presents a different set of problems and opportunities for those living and thriving with HIV. This begs the question as to whether successful aging with HIV is possible. It is; however, it depends upon the definition of successful aging. This presentation reviews the components of successful aging as it relates to HIV. Specifically, the following will be examined: Length of life, biological health, mental health, cognitive efficiency, social competence, personal control, and life satisfaction.

Changes in the perception-action synergy as a function of Dementia

Professor Michael Wade, University of Minnesota twin Cities Campus, Minneapolis, United States

The effect of cognitive deficits and its impact on postural motion in three age matched groups of older adults was investigated. The hypothesis was that individuals with cognitive deficits will show higher variability of postural motion when engaged in a visual task which comprised two conditions. A control condition (BT)-where participant's looked anywhere within a blank white target;and an experimental condition (CT)-where participant's counted the frequency of a designated alphabet letter, within a stream of random letters. The significance of this investigation was the established relationship between cognitive deficits and postural motion. This embodied relationship may serve as a diagnostic tool for early onset dementia.

Day 1:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

STRATEGIES TO DELAY CELL SENESCENCE: BACK TO THE BASICS OF CELL BIOLOGY

Hani Atamna
College of Medicine, California University of Science & Medicine, Colton, CA 92324 atamnah@calmedu.org

Abstract:
Accumulating in vivo evidence indicates that the increase in number of accumulating senescent cells with time could play a role in the aging process. Senescent cells are dysfunctional and secrete factors that interfere with the function of normal cells in their vicinity. Thus, delaying cell senescence may be a viable strategy to modulate the physical and cognitive decline that occurs with age. Our research efforts in this direction identified Diaminophenothiazines (e.g., methylene blue, MB) as a potent anti-senescence agent, exceeding any other agent in this category. At very low concentrations MB delays cellular senescence causing >50 % gain in Population Doubling Levels (PDL) and prolongs the cell culture lifespan by six weeks (47%) beyond the control. In order to identify possible pathways that are important for cell senescence we investigated the metabolic pathways that may be targeted by MB. Our research in this direction revealed that the mild redox activity of MB plays a significant role in its mechanism of action. At the molecular level MB caused: 1) transient increases in NAD/NADH and pAMPK/AMPK ratios. This effect is followed by the induction of PGC1 and SURF1; both factors are essential for mitochondrial and complex-IV biogenesis. This action explains the high reserve of complex-IV activity and mitochondrial mass in MB-treated cells as well as the decline in the production of intracellular oxidants. 2) MB activates the cellular defense system Keap1/Nrf2. This explains the increased resistance of the cell to hydrogen peroxide as well as other toxins. 3) surprisingly, MB was found to lower the intracellular "free heme" by 50%, an effect that should lower the steady-state level of oxidative damage to macromolecules and consequently enhance their stability. This is consistent with the finding that the rate of telomere erosion was 8-times slower in MB-treated cells. Collectively, these results indicate that MB engages multiple biochemical pathways that team to enhance cellular metabolism, cell defense systems, while lowering mediators of oxidative damage (e.g., free heme and oxidants). These findings are consistent with the notion that aging is multifactorial and affects various cellular systems. Therefore, an agent that simultaneously activates several pathways may be considered as having a favorable value as an anti-senescent drug. It is important to emphasize that MB lacked an effect on the cell cycle, thus an MB-dependent cell cycle change is unlikely to contribute to its anti-senescence activity. These findings will be presented in the context of a novel model that incorporates organ reserve, metabolic capacity, and cell senescence.

MULTIPLE CYTOKINE ANALYSIS OF INFLAMMAGEING IN NORMAL AGEING AND WERNER SYNDROME

M. Goto, K. Hayata, J. Chiba, M. Matsuura

Introduction & Aims: Human ageing is inevitably accompanied by an increasing chance of a variety of stress from inside (e.g. ER stress, mutation, hypoxia, immune-surveillance -associated proteins and genetics/epi-genetics) and outside (e.g. UV, air pollution, allergens, infectious agents, drugs and foods), leading to a minor inflammation-driven inflammageing' that can be roughly evaluated by highly sensitive CRP (hsCRP). We have been studying mechanism(s) of ageing by comparing normal Japanese individuals, Japanese rheumatoid arthritis and Japanese Werner syndrome (WS: MIM #27770). The purpose of the study is to clarify; 1). Do normal individuals and Werner syndrome age with inflammation evaluated by hsCRP ? and 2). Which cytokines are associated with ageing in normal population and WS?

Methods: A total of 217 normal Japanese sera between 1 and 100 years old and 41 mutation-proven WS (between 32 and 70 years old) from both sexes were used. All of the individuals provided written informed consent for the study, which was approved by the Ethical Committee of Toin University of

Yokohama. All of the samples were stored -80°C until use. Elderly normal individuals met for the SENIEUR criteria were selected.

1) The serum hsCRP was measured by CircuLex high-sensitivity CRP ELISA kit. 2) 26 cytokines (IL-1β,IL-1ra, IL-2, -4, -5, -6, -7, -8 (CXCL8), -9, -10, -12, -13, -15, -17, basic FGF, G-CSF, GM-CSF, PDGF, VEGF, TNFα, IFNγ, IP-10 (CxCL10), MCP-1 (CCL2), MIP-1α(CCL3), MIP-1β(CCL4) and eotaxin (CCL11) were simultaneously measured by using Bio-Plex suspension multiplex array system.

Data analysis & Statistics: Ageing-associated changes of serum levels of hsCRP or cytokine were examined by using non-linear regression model expressed as hsCRP = exp (a + b*Age + c*Sex), where a, b, and c are estimated regression coefficients. or log_e(cytokine (j))= a + b*Age + c*Sex, where a is an estimated intercept, b and c are estimated regression coefficients and j is an indicator for individual cytokine. Differences of hsCRP between two groups (normal adult aged between 25 and 70 years (NA) vs normal elderly aged between 71 and 100 years (NE) or NA vs WS) were tested by two-sample t-test with unequal variances.

Results & conclusions: The serum level of hsCRP increased significantly ($p<0.001$) with normal ageing without gender difference. Significant normal ageing-associated increases were observed on IL-4 ($p=0.005$), IL-6 ($p=0.011$), IL-13 ($p<0.001$), IL-15 ($p<0.001$), GM-CSF ($p<0.001$), IFN-γ ($p=0.037$), TNF-α ($p=0.04$) and IP-10 ($p<0.001$), while IL-8 ($p=0.003$), MIP-1α ($p<0.001$) and IL-2 ($p=0.003$) levels were significantly decreased with normal ageing. The serum hsCRP did not correlate with calendar ageing in WS, though the hsCRP level (mean±SD; 11.0±1.6 μg/ml) elevated significantly compared with age-matched NA (1.3±0.3 μg/ml) and NE (4.2±0.7 μg/ml), respectively ($p<0.001$). No sex-difference was on the serum hsCRP level in WS. Although none of the 26 cytokines/ chemokines associated with calendar ageing in WS, IL-4 ($p=0.008$), IL-6 ($p<0.001$), IL-15 ($p<0.001$), GM-CSF ($p<0.001$), MCP-1 ($p=0.008$), TNF-α ($p=0.002$), IL-10 ($p=0.031$), basicFGF ($p<0.001$), G-CSF ($p<0.001$), IFN-γ ($p=0.021$) and IL-2 ($p=0.029$) levels were significantly increased compared with age-matched NA. The immunological-shift to Th2 (IL-4, IL-6, IL-10 and GM-CSF) in WS was similar to the Th2-biased cytokine changes (IL-4, IL-6, IL-13 and GM-CSF) in normal ageing. Further study may warrant the pathophysiology of Th2-biased inflammageing.

CARBAMYLATION, A NONENZYMATIC POSTTRANSLATIONAL MODIFICATION OF PROTEINS ASSOCIATED WITH LONGEVITY

L. Gorisse, C. Pietrement, V. Vuiblet, C.E. Schmelzer, M. Köhler,
L. Duca, L. Debelle, P. Fornes, S. Jaisson, P. Gillery
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Ageing is associated with tissue alterations, which may be explained by nonenzymatic post-translational modifications (e.g. glycation, oxidation, carbamylation) of proteins. Some pathological contexts like diabetes, vascular diseases or renal failure are known for amplifying these chemical modifications. A still poorly investigated reaction is carbamylation, which corresponds to the binding of isocyanic acid, a urea by-product, to protein amino groups. This process leads to the formation of carbamylationderived products (CDPs) including homocitrulline (HCit), which results from lysine carbamylation. *In vitro* experiments have shown that carbamylation contributes to the alteration of structural and functional properties of proteins. However, the metabolic fate of carbamylated proteins *in vivo* is still unclear, especially during ageing. In this study, we have evaluated the tissue accumulation of CDPs over the time in three mammalian species. We have observed that HCit concentrations progressively increased in murine tissues from birth to 2 years, the highest content being noted in skin. The same evolution was observed in bovine and human skin, with an elevation of 11.5 and 8.1-fold between the young and old subjects, respectively. Interestingly, this reaction impacts more intensely matrix proteins, probably because of their long half-life. Indeed, skin type I collagen and elastin were significantly carbamylated in oldest subjects compared to youngest ones. These results showed that carbamylation is a physiological reaction associated with ageing, which leads to an accumulation of CDPs in tissues. Such modifications could induce turnover alterations and cellular dysfunctions contributing to agerelated complications.

GENETICS AND HERITABILITY IN HUMAN LONGEVITY: INSIGHTS FROM UK BIOBANK

LC Pilling, A Wood, S Jones, R Beaumont, J Tyrrell, M Tuke, K Ruth, H Yaghootkar, R Freathy, LW Harries, A Murray, M Weedon, T Frayling, D Melzer*
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Introduction: Later age at death of parents is associated with delayed onset of age-related diseases in humans (Dutta et al. 2013). However, very few genetic variants have been discovered associated with longevity (Shadyab and LaCroix 2015) despite the evidence for genetic enrichment in long-lived individuals (Schoenmaker et al. 2006) . We are interrogating the UK BioBank data for genetic markers associated with age-at-death of the parents of the participants.

Methods: Analysis of 45,000 UK BioBank participants aged between 60-69 with genotype data and reported age-at-death for both parents. Participants were categorized based on the age-at-death of their parents (e.g. "two long-lived parents", "two short-lived parents"). Genome-wide association studies were performed on the directly genotyped polymorphisms (n=850,000) and genetic heritability estimates were determined.

Results: Preliminary analyses have revealed promising markers for "father's age at death" that await confirmation and further investigation. Analyses into the parental longevity score are ongoing (Aug 2015), with results due prior to the conference (Feb 2016).

Conclusions: This preliminary analysis on the pilot genetic data is revealing potentially novel signals, which we will investigate and report at the meeting. Once the full data is released (approximately tripling our current sample size) the statistical power will also increase, allowing further investigation into the genetics of longevity.

Dutta, Ambarish et al. 2013. "Longer Lived Parents: Protective Associations with Cancer Incidence and Overall Mortality." Journals of Gerontology - Series A Biological Sciences and Medical Sciences 68(11):1409–18.

Schoenmaker, Manja et al. 2006. "Evidence of Genetic Enrichment for Exceptional Survival Using a Family Approach: The Leiden Longevity Study." European journal of human genetics : EJHG 14(1):79–84.

Shadyab, Aladdin H., and Andrea Z. LaCroix. 2015. "Genetic Factors Associated with Longevity: A Review of Recent Findings." Ageing Research Reviews 19:1–7.

Day 2:

Oral Presentation Abstracts

EXPLORING THE ROLE OF SOCIAL PARTICIPATION IN OLDER PEOPLE WITH MUSCULOSKELETAL PAIN: A FOCUS GROUP STUDY

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Background:
Musculoskeletal pain affects over 70% of those aged 50 years or over, and is associated with poor health, increased disability and increased primary care consultation. Social participation, defined as engagement in social activities and the fulfilment of social roles, is an important component of quality of life in older people, and consequently an important health outcome in older people with musculoskeletal pain. Older people with musculoskeletal pain, who maintain social participation, are

more likely to report better health outcomes (e.g. reduced levels of depression and better cardiovascular health) than those who report social participation restriction. The aim of this study was to explore the ways in which older people who report good health, whilst experiencing musculoskeletal pain, perceive social participation to contribute towards their health.

Methods:
Focus group of retirement village residents in the West Midlands, who reported troublesome pain, maintaining social participation and having good health (n=6; all female). A template analysis approach was used to synthesise the focus group data into themes, exploring how social participation contributed towards participants' perceived good health. An exploratory model of the relationship between pain and self-reported good health was then developed.

Results:
Pain was infrequently mentioned in the focus group discussion, except in terms of associated disability and experiences of management strategies, including analgesics. Reported social participation activities differed between participants; however the group members shared common opinions of the benefits of social participation (e.g. fulfilling the need to get out of the confines of the village and accessing social support). Personal characteristics (e.g. positive mental attitude and self-efficacy), sense of place (e.g. social embeddedness within the residential village) and environmental factors (e.g. transport accessibility and provision of instrumental support from staff) emerged as key themes which contributed to the relationship between social participation and good health.

Conclusions:
A model will be presented to illustrate how best to support older people with musculoskeletal pain to maintain their health by reducing the impact of painful conditions on individual wellbeing, and wider society. Encouraging older people to increase or maintain social participation is a potentially useful approach, but needs to take account of individual characteristics and circumstances and environmental factors.

GERONTOLOGY: A FUTURE CAREER CHOICE IN HEALTH AND SOCIAL CARE?

Coffey, A., McCarthy, G., O'Mahony A., M Arola., S. Auer., E. Corvo., D. Deimante-Hartmane., U. Gaidys., C Petersen- Ewert., J. Sansoni., Mikkonen, I (2015).
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Background: As global populations age, the need for health and social care professionals working with older people is of increasing interest. However little reliable research has examined students perceptions of working with older people.

Aim: To measure the attitudes of health and social care students towards older people, along with perceptions of working with older people.

Methodology: Undergraduate health and social care students (n=955) from 5 European countries in their final year of study completed a demographic questionnaire; Attitudes towards Older People Scale (Kogan1966) and Students' Perception of Working with Older People Scale (revised) (Nolan et al, 2006).
Findings: Respondents were generally positive towards older people with the majority agreeing that working with older people was skilled, challenging and stimulating. However, a significant number of students disagreed (19%) or neither agreed nor disagreed (31%) to definitely choosing a career working with older people when they qualified. Additionally, 20% disagreed that working with older people held high status, with a further 42% were unsure. Significant relationships existed between positive experiences with older people prior to commencing an educational programme, and favourable disposition towards working with older people.

Conclusion: Students indecision about working with older people suggests the need for robust promotion of gerontology as a clear and appealing career pathway in health and social care.

THE IN VIVO AND IN VITRO NEUROPROTECTIVE EFFECTS OF INNOVATIVE CHINESE MEDICINE FORMULA AGAINST DEMENTIA

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Abstract:

Health burden raising from ageing is becoming apparent in last few decades. Currently, ageing-related neurodegenerative diseases such as Alzheimer's disease (AD) and vascular dementia are the two most common types of dementia. They are incurable but the emerged symptoms can only be slowed down [1]. The currently used drugs on dementia aim to regulate neurotransmitters. However, these medications are not targeting on the pathological processes of dementia including oxidation [2] and β-amyloid cascade [3], etc. The chemical components and organic extracts of Traditional Chinese Medicines (TCM) such as Tianma (TM) and Danshen (DS) have been reported to have neuroprotective effects. However, the effects of these water extract are not well-studied.

Based on previous works on single herb water extract and different concentration ratio of DS and TM, we have selected DS and TM in the ratio of 2:1 and this combination was named as DT formula. The objective of our study was to investigate the neuroprotective effects of DT formula using in vivo middle cerebral artery occlusion (MCAO) rat model to mimic the ischemic stroke condition, which is the major cause of vascular dementia. Besides, we also studied the effect of DT formula against AD using 5xFAD transgenic mice model. The underlying mechanisms were further investigated using various in vitro platforms including oxygen-glucose deprivation/reperfusion model (OGD/R), β-amyloid induced cell death and inhibition of acetylcholinesterase activity.

The SD rats were subjected to MCAO for 2 hours and followed by 24 hours reperfusion. The treatments were orally administered 1 hour before the MCAO. Our results demonstrated that low dose (1.067 g/kg) and high dose (2.134 g/kg) DT formula could significantly ameliorate the neurological deficit of MCAO-operated rats from 2.58 to 1.91 ($p<0.05$) and 1 ($p<0.001$), respectively. The brain infarct volume was significantly decreased from 0.42 cm3 to 0.21 cm3 ($p<0.01$) and 0.13 cm3 ($p<0.001$) after oral administration of low dose and high dose of DT, respectively. The activities of anti-oxidative enzymes (glutathione peroxidase and superoxide dismutase) in MCAO-operated rats were enhanced significantly ($p<0.05$) by DT formula. The anti-inflammatory effects of DT formula was revealed by the significant inhibition of inflammatory cytokines (TNF-α and IL-6) production after MCAO. Besides, we also studied the neuroprotective effects of DT formula using 5xFAD transgenic Alzheimer's disease mice. The treatment was started with the 4 months old mice by oral administration and lasted for 8 weeks. The learning ability and spatial memory of the mice were assessed using Morris Water Maze (MWM). From the MWM, the preliminary results showed that 2.1 mg/kg and 4.2 mg/kg of DT treatment on 5xFAD would improve the performance in platform searching (i.e. lower latency) during the acquisition training and more island entries when compared with the control group during the probe test. We further elucidated the neuroprotective mechanisms of DT formula using OGD/R on PC12 cell line for vascular dementia. We also studied β-amyloid induced toxicity as well as the inhibitory effects of DT formula on acetylcholinesterase activity on PC12 cell line. DT formula was found to ameliorate β-amyloid-induced cell death from 42% to 61% ($p<0.001$). Our results also demonstrated that DT formula at 500 μg/ml showed the most significant attenuation of β-amyloid-induced toxicity on PC12 cells by 21% ($p<0.001$) and also inhibited acetylcholinesterase activity by 26% ($p<0.001$).

The neuroprotective effect of DT formula towards cerebral ischemia and reperfusion damage was demonstrated using the in vivo MCAO rat model and in vitro OGD/R model. These findings suggested that DT formula may protect neuronal cell death due to cerebral ischemia and reperfusion injury, which may consequently lead to vascular dementia. β-amyloid deposition and cholinergic deficit are major pathological events in AD. The results from in vitro studies provided the evidence of using DT formula to tackle this situation. Furthermore, the preliminary result from in vivo MWM also revealed that the DT formula may provide a modulatory effect in Alzheimer's disease.

In conclusion, we are the first group investigating the effects of DS and TM water extracts towards dementia. Our study also provided the first scientific evidence showing DT formula having anti-oxidative, anti-inflammatory, anti-β-amyloid-induced toxicity as well as the inhibitory effects on acetylcholinesterase activity. All these effects accounts for the neuroprotection against cerebral ischemia and reperfusion induced vascular dementia in the MCAO rat model as well as the 5xFAD AD mice model. Our results suggested the potential use of this innovative formula as a herbal supplement for elderly with dementia.

References:
[1] Ho YS, et al., (2011). Drug discovery from Chinese medicine against neurodegeneration in Alzheimer's and vascular dementia. Chin Med. 6:15.
[2] Aldred S. (2009). Oxidative stress in vascular dementia and Alzheimer's disease: a common pathology. J Alzheimers Dis. 17(2):245-57.
[3] Selkoe DJ, et al., (2002). The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. Science 297(5580):353-6.

BEREAVEMENT FINDINGS FOR NEEDED DEVELOPMENTS

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Older people often experience the deaths of family members and friends. Illnesses and premature death are proven outcomes of bereavement. Evidence is lacking however to establish bereavement as a major social/health issue needing attention. A study was done using a random-dialing telephone system for population-based answers from 1208 adult Albertans to a series of questions. Findings: 96% reported having felt grief at least once (median times = 5), 31% experienced a death causing grief in the last year and another 15% in the last 1-2 years, and 78% reported feeling grief now. The mean score for perceived quality of death/dying was 5.9 – it was slightly more good than bad. Only 22% obtained help. In adjusted analyses, bereavement grief was higher when the respondent was female, Protestant or Catholic, when the death grieved over was <2 years ago, and it involved a spouse/parent/child. Bereavement grief was lower when the perceived death/dying quality was higher. The odds of obtaining help were higher among females, when the deceased was a child, and when more severe grief was reported. The odds of obtaining help were lower when the perceived quality was higher. As such, bereavement grief is common, and personal and situational factors appear to impact the intensity of grief and likely also the impact of grief. Further research is needed to confirm these findings and to ensure that accessible evidence-based formal and informal bereavement supports exist.

Day 3:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

ROLE OF ANTI-INFLAMMATORY CYTOKINES ON MUSCLE MASS AND PERFORMANCE CHANGES IN ELDERLY MALES AND FEMALES

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Aging has been frequently associated with an increased baseline level of pro-inflammatory cytokines, which are believed to partially explain the age-related alterations in muscle mass and strength, but only a few studies investigated the role of systemic anti-inflammatory cytokines levels in the skeletal muscle homeostasis in older individuals.

The study included 120 subjects, 92 women and 28 men aged 72,27±2,06 years (mean±SD) and with BMI of 26,52±4,07 kg/m2 (mean±SD) at baseline. Six minutes walking test (6MWT) and Dual Energy X-ray absorptiometry (DXA) evaluation, with total, appendicular, and legs fat free mass (FFM) determinations, were obtained at baseline and after 4,5 years of mean follow-up. Height, weight, body mass index (BMI), nutritional status, physical activity level, comorbidity and TNFα, IL-4, IL-10, IL-13 circulating levels were evaluated at baseline.

Our study group presented a significant reduction of appendicular FFM and 6MWT performance (all $p < 0.001$) after 4.5 years follow-up. Moreover, in a stepwise regression model, considering appendicular FFM decline as dependent variable, and gender, age, BMI, nutritional status, physical activity level, comorbidity, baseline FFM, basal level of IL-10, IL-13, IL-4 and TNFα as independent variables, we found that the proportion of variance explained by IL-4, BMI, baseline appendicular FFM, TNF-a and IL-13 was 14.2%, 21.3%, 25.8%, 28.8% and 30.8%, respectively. Additionally, when considering 6MWT decline as dependent variable, and the same independent variables, the proportion of variance explained by baseline walking test performance was 9.8%, while adding IL-13 and TNFα the proportion reached 18.5% and 22.9% of variance.

The data of these prospective, population-based study suggest that higher serum levels of anti-inflammatory markers , and in particular IL-4 and IL-13, may play a protective role on FFM and performance maintenance in elderly subjects, independently of age, sex, BMI and TNFα levels.

BIG DATA ON LONGEVITY IN A FOUNDER POPULATION

Sandra P. Smieszek

Big data and integration of series of omics technologies carry great potential for elucidating the genetic underpinnings of longevity, hence healthy aging. Unfortunately, while genome-wide association studies using unrelated individuals have revealed many interesting aging associated variants, these variants are typically of small effect and cannot explain the observed patterns of heritability for this complex trait. Even though there is great potential in large scale approaches, none so far have produced reproducible results. In contrast numerous successful examples exist for elucidating the highly penetrant rare segregating alleles that have been discovered using family based approaches. Furthermore, family based approaches have other advantages: the ability to overcome confounding factors such as population stratification. We conducted a family based approach to longevity using founder population of the Amish community in central Ohio. As the heritability of longevity is estimated be 40 percent it is a highly interesting research domain in this population. Our design study using a single large multi-generation pedigree to directly measure heritability together with phenotypic traits and epigenetic variation is unique and powerful. The genetics have an added layer of complexity at all stages from design to analysis nevertheless the findings are of high value. Heritability was assessed using multiple contrasts:

parent-child, mid-parent-child sibling-sibling and grandparent-grandchild. The present approach integrates both phenotypic and genotypic approach which has led to discovery of a series of variants, distinct for stratified population across ages and distinct for paternal and maternal cohorts. The potential significance of this study is profound.

CHANGES IN MORBIDITY BY PROXIMITY TO DEATH OVER TIME: EVIDENCE FROM EUROPE

Over the years, life expectancy has increased significantly in the EU. Whether the additional life time is spent in good or in poor health will drastically influence the development of health care costs as morbidity status rather than age per se determines an individual's need for health services. However, empirical evidence on whether the prolonged lifespan is associated with a compression or an extension of morbidity is still sparse and inconclusive. In this paper, we analyse the prevalence of disability in the population 50+ in Europe by age and by proximity to death over time using longitudinal data from the Survey of Health, Ageing, and Retirement in Europe (SHARE). Despite an ageing population, we find average disability levels to remain constant over time. However, disability levels close to death increases.

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Poster Presentation Abstracts

Poster abstracts will be finalised weeks before the event

AN ELDERLY PERSON - A VIOLENT PERSON

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INTRODUCTION

Research regarding violence related with elderly people frequently concern violence against seniors; there are very few analyses regarding elderly people as the ones who use violence. The research conducted shows that elderly people do use violence, usually in their marriage.

AIM

The aim of the research was to examine the phenomenon of violence used by elderly people within the area of the Szczecin City Municipality.

RESEARCH MATERIAL AND METHOD

1299 Blue Cards registered in 2012 and 2013 in the Szczecin City Municipality were analysed. The research included 114 cards concerning elderly people as the ones using violence. The analysed group consisted of 10 women (8,8%) and 104 men (91,2%).

RESULTS OF THE RESEARCH

Elderly people used violence significantly more frequently against women (n=99;86,8%), often their wives (n=60;52,6%). The dominant period of using violence was between 1 and 3 years. The most frequent form of physical violence used by elderly people was pushing (n=92;80,7%), and psychological violence - insults (n=103;90,3%). Sexual violence was used by 7 of the examined people (6,1%), and other types of behaviour included threats (n=72;63,1%). After a violent incident, the person using violence was usually aggressive (n=51;44,7%). Alcohol abuse was noted in as many as 83 of the examined people (72,8%). The most frequent action taken by the police against a violent person was taking them to a sobering station (n=57;50%).

CONCLUSIONS

1.Gender has significant influence on the character of violence used. Men use violence more frequently, and women are usually the victims of violence.
2.Substance abuse is strongly related with using violence.

TOOTH LOSS, CHEWING ABILITY AND QUALITY OF PROSTHETIC APPLIANCES IN A GROUP OF ELDELY HOME RESIDENTS FROM NORTHERN CROATIA

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ABSTRACT

Aim: The aim of this study was to clarify the relationship between tooth loss, quality and types of prosthodontic appliances and their impact on chewing performance and food choice in elderly.
Material and methods: In this study 110 geriatric care home residents from northern Croatia participated between the age of 64 and 98. Informed consent was taken for all the subjects and privacy and confidentiality of the information were maintained. Each examinee completed a questionnaire after which an oral examination was performed. Obtained data included dental and medical history, tooth loos, assessment of prosthodontic appliances by CDA Quality Index, Chewing Ability Index according to Yoshida et al.,and oral hygiene assessment.

Results: From total number of participants 78 % were female and 22 % male participants. Edentulous or subtotal edentulous with 25 or more extracted teeth were 54 % of the examinees. Some type of prosthodontic appliances had 84% of subjects , most commonly complete and /or partial dentures (68%). According to CDA Index of Quality , 46 % of all examined prosthodontic appliances were in need

for replacement, among them 16 % for immediate replacement. Up to 10 years old were 63% of the appliances, and the oldest was 50 years old. Chewing ability assessed according to Yoshida et al. demonstrated that only 32 % of examinees were able to chew all types of food, but mostly slow, while 20 % of them were able to eat liquid food only.

Conclusion:. Extensive tooth loss, inadequate quality status of prosthodontic appliances, or lack of them at all, influenced the chewing ability of the tested examinees.This is one of the reasons for inadequate nutritional status in elderly, which can affect maintenance of good health, physical power and activity. Population of the elderly is rapidly increasing and it is important to emphasize the importance of maintaining good oral health to achieve good quality of life.

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VISITOR RESTRICTION POLICIES AND PRACTICES IN NURSING HOMES

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An online survey gathered information on organizational policies and practices for restricting or banning visitors from nursing homes in Alberta. All 27 members of the Alberta Continuing Care Association were invited to respond anonymously. Findings: 25% of respondents indicated a visitor is currently banned, 33.3% indicated a visitor had been banned from their facility at some point in the past (1 to 4 times each), 66.7% have restricted a visitor in the past, such as through mandated supervised visits or time restrictions. The most common reason was their staff needed it, either with staff abuse or the potential for physical and emotional abuse. Restricting or banning a visitor was also done upon resident request. One facility reported a written policy, with 3 having unwritten policies. The facility with a policy was said to have "some challenging visitors" and the "staff needed structure and continuity to keep consistency and equity." Another respondent indicated they "may consider developing one in the future as we are seeing visitor issues happening at other sites." As such, continuing care visitor restriction policies and practices do not appear to be common, but they are evident. The large numbers of continuing care residents and visitors indicates future developments in visitor management and visitor rights are likely.

DEVELOPMENT OF AN EARLY PRE-MOTOR ROTENONE MODEL OF PARKINSON'S DISEASE

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Parkinson's disease (PD) is a severely disabling condition, with only limited treatment options and no drugs available to slow or halt disease progression. At the time patients present with motor symptoms approximately 50% of the dopaminergic neurons in the substantia nigra (SN) have already been lost. Tyrosine hydroxylase (TH), the rate limiting-enzyme in catecholamine synthesis, is also lost when these cell die. PD patients also suffer from numerous non-motor symptoms such as constipation and depression that they report to have a greater impact on their quality of life than the typical motor symptoms. In this study we aimed to investigate how well rotenone can model the motor and gastrointestinal (GI) symptoms and TH changes observed in PD.

Male Sprague-Dawley rats received intraperitoneal injections (2.75 mg/kg) of rotenone (n=7) or vehicle (n=6) 5 days/week for 4 weeks. The rearing and rotarod behavioural tests were performed fortnightly. Rats were fasted overnight prior to tissue collection to assess their gastric emptying capacity. Adrenal glands, colon and selected brain regions were collected *postmortem* for western blot analysis of TH protein.

The rearing test, which assess voluntary movement, showed reductions in the rotenone group by week 2 ($p<0.0001$) and week 4 ($p<0.0001$), whereas no changes were found in the rotarod test, which assesses forced movement. The gastric emptying test demonstrated slowing of GI motility as the rotenone group had more contents remaining in the stomach, small intestine and colon after overnight fasting. In the SN

we detected approximately a 25% reduction in TH (p=0.003). In the periphery we found a 2.5 fold increase of TH in the adrenal gland (p=0.002) and trend for decreased TH in the colon.
This rotenone dosing paradigm may have potential to model the early pre-motor stage of PD as it induces loss of TH in the SN below the threshold of that which causes motor symptoms. This paradigm also induces functional changes in the GI system similar to the constipation that is evident in many PD patients' years before the motor symptoms develop.

CONSTIPATION IN PARKINSON'S DISEASE: A REVIEW OF EVIEDNCE-BASED TREATMENTS OF AND THE ROLE OF THE PHARMACIST

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Background: The wide array of non-motor symptoms in Parkinson's disease are often under-recognised and therefore undertreated. Patients report such non-motor symptoms to have a greater burden on their day-to-day life than the motor-symptoms. Constipation is an exceedingly common non-motor symptom in Parkinson's disease, reportedly affecting up to 70% of patients. The two main causes of constipation in Parkinson's disease are slow colonic transit and defecatory dysfunction. The development of Lewy body pathology in the enteric nervous system is thought to play a role in the slow colonic transit observed in Parkinson's disease. As the pathology of constipation in this patient population may differ from other presentations of chronic constipation, management should include treatments that have been evaluated specifically in this patient group.

Pharmacists are ideally positioned to screen patients with Parkinson's disease for constipation and to recommend evidence-based treatments to optimise the management of constipation. This review aims to describe the evidence for different treatments in the management of constipation in patients with Parkinson's disease, and to provide commentary regarding the role of the pharmacist in optimising the management of constipation in this setting.

Methods: Papers for review were identified through an electronic search of PubMed, Embase and Web of Science databases using the following search terms: "constipation" OR "gastrointestinal dysfunction" OR "slow colonic transit" OR "defecatory dysfunction" OR "slow motility" AND "treatment" OR "management" OR "therapy" AND "Parkinson* disease". Reference lists of articles identified through initial search were then reviewed to identify any additional articles of relevance.

Review findings: Macrogol (polyethylene glycol) is a safe and effective treatment for constipation in patients with Parkinson's disease; it should be considered a first line treatment option and can be recommended by the pharmacist over-the-counter. Pharmacists can provide information regarding fibre supplementation with psyllium, which may also be effective and can be initiated early. If over-the-counter options fail the pharmacist should be familiar with the suitable prescription treatments for this condition. Lubiprostone appears to be a promising option for managing constipation in Parkinson's disease, but larger trials with a longer duration of treatment are warranted. It remains to be determined if newer drugs such as the 5-HT_4 agonist prucalopride or the guanylate cyclase C receptor agonist linaclotide will prove beneficial in treating constipation in the Parkinson's population.

Conclusions: Although many commonly employed treatments for constipation have not been evaluated for efficacy in Parkinson's disease, pharmacists can utilise available data to make evidence-based recommendations, optimise constipation management, and improve the quality of life for patients with Parkinson's disease.

PARENTAL LONGEVITY IS ASSOCIATED WITH A LOWER OFFSPRING RISK OF MORBIDITY AND MORTALITY IN THE UK BIOBANK STUDY

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Introduction: The offspring of longer-lived parents have a lower risk of several age-related morbidities and mortality. We are studying the mechanisms of longevity by estimating the associations between the age at death of the parents of study participants, and risk of incident disease and mortality in middle to older aged UK adults.

Methods: Prospective data from the UK Biobank was available for 189,076 participants aged 55-73 years. Mother's and father's age at death was used to generate a ranked parental longevity score, with a higher score indicating a greater parental age at death. Participants were followed-up from baseline for mortality and morbidity for a mean period of 5.5 years and 6 years respectively. Cox proportional hazards regression models investigated the associations of parental longevity score and the risk of incident disease and mortality. Models were adjusted for potential confounders including age, sex, ethnicity, education, income, smoking status, alcohol intake, physical activity and body mass index.

Results: Increasing parental longevity score was associated with a lower risk of incident disease during follow-up, including diseases of the cardiovascular system, respiratory system and cancer. Offspring with longer-lived parents also had a lower risk of all-cause mortality (HR per increase in parental longevity category: 0.87, 95% CI: 0.84-0.91), CHD mortality (HR: 0.74, 95% CI: 0.65-0.83) and cancer mortality (HR: 0.89, 95% CI: 0.85-0.94) after adjustment for confounders. However, no trend was observed for stroke-related mortality.

Conclusion: Data from the UK Biobank provides robust evidence that higher parental longevity is associated with a lower risk of cardiovascular, respiratory and cancer morbidity and a lower risk of mortality from all-causes, coronary heart disease and cancer in offspring.

ANALYSIS OF ZEB1 CONTRIBUTION TOWARDS THE PATHOGENESIS OF FUCHS' ENDOTHELIAL CORNEAL DYSTROPHY

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PURPOSE: To scan the zinc finger E-box binding homeobox 1 (ZEB1) gene for mutations or polymorphic markers that are associated with the Fuchs' endothelial corneal dystrophy (FECD), affecting several Indians above 40 years of age; and to determine its role in the development of FECD by regulating Collagen, Type VIII, Alpha 2 (COL8A2) gene.

METHODS: Genomic DNA was extracted from peripheral leucocytes of 62 FECD patients and 128 unrelated controls. ZEB1 exons including the intron- exon boundaries were sequenced bi-directionally by Sanger sequencing method. The association of polymorphisms was analyzed using $\chi 2$ test and logistic regression. Biotin labeled oligos of COL8A2 promoter proximal regions comprising conserved E-box motifs were employed along with the nuclear extracts of primary human corneal epithelial cells (HCEC) that were taken as ZEB1 protein source for electromobility shift assay (EMSA).

RESULTS: Exon scan of ZEB1 gene showed a significant novel association of rs220057 (Df1, P = 0.032; Df2, P = 0.015) with the sample Indian FECD population. However, the previously reported mutations in ZEB1 gene of Caucasian FECD families were not found in our study population. Competitive and

supershift EMSAs confirmed that ZEB1 from the nuclear extract of HCEC bind to the E-box motif present at the proximal region of COL8A2 promoter.

CONCLUSIONS: This is the first report identifying a polymorphic marker for ZEB1 gene in significant association with sporadic FECD cases, thereby rendering a stronger genetic load upon ZEB1 for being a causative agent for the disease. Further studies are required to identify the exact role of rs220057 in disease causation. This is the first evidence of ZEB1 binding to the promoter proximal region of COL8A2 through in vitro DNA binding assays. COL8A2 have been previously reported to show heavy deposition in the Descemet's membrane of FECD tissues. Examining the expression levels of ZEB1 and COL8A2 in FECD and control tissue samples may help understand its role in disease pathogenesis.

OSTEOCYTE-SPECIFIC CAS KNOCKOUT MICE EXHIBIT DECREASED BONE MASS THROUGH INCREASED OSTEOCLASTIC BONE RESORPTION

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The skeleton is a metabolically active organ that undergoes continuous remodeling throughout life. Osteoporosis, which is fostered by advancing age, is the most common clinical disorder affecting bones. Although it has been postulated that osteocytes play an important role in sensing mechanical load in bone tissues, detailed molecular mechanisms of how osteocytes regulate bone metabolism remain largely unclear.
The adaptor molecule p130Cas (Crk-associated substrate, hereafter referred to as Cas), which is phosphorylated at focal adhesions upon extracellular matrix engagement, is involved in various cellular processes including migration, survival, transformation, and invasion. In addition, we reported that Cas binds to the cytoskeletons in a stretch-dependent manner. This suggests that Cas can function as an initiator of intracellular signaling cascades through force-dependent changes in the cytoskeleton network.
To investigate the role of Cas in bone metabolism, we generated osteocyte-specific Cas conditional knockout (cKO) mice by mating Casflox/flox mice with Dentin matrix protein 1 (Dmp1)-Cre transgenic mice, in which the Cre recombinase gene was specifically expressed in osteocytes. The resulting Dmp1-Cre+/−;Casflox/flox mice (referred to herein as Cas cKO mice) exhibited a significant decrease in bone volume, as determined by μCT analysis. Histomorphometric analysis of Cas cKO mice revealed a significant increase in the eroded surface/bone surface ratio, osteoclast surface, and osteoclast number. Furthermore, the expression levels of RANKL genes were significantly increased in the osteocyte fractions derived from Cas cKO mice. Collectively, these findings suggest that the bone loss in Cas cKO mice was caused by increased osteoclatstic bone resorption.

THE ASSOCIATION BETWEEN LEVELS OF BLOOD MERCURY AND DEMENTIA: A CASE-CONTROLS STUDY IN TAIWAN

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Previous literatures showed that the levels of blood mercury in the Taiwan population were higher than other nations. However, few studies have examined the impact of human chronic exposure to mercury during the aging process. Therefore, the purpose in the present study was to assess the association between levels of blood mercury and dementia and further elucidate the possible exposure source of mercury. We constructed a case-control study, consisting of healthy controls, people with mild cognitive impairment (MCI) and dementia patients who included new incidence and prevalence cases. All subjects underwent neuropsychological evaluations by psychiatrists, including the Mini-Mental State Examination (MMSE) and the Clinical Dementia Rating (CDR) scale. Diagnosis of dementia was identified using ICD-9 code, including the diagnosis codes 290.x, 294.1, and 331.0. The healthy control subjects had a CDR score of 0 and the MCI subjects had a CDR score of 0.5, and subjective memory complaints. In addition, they were invited to receive a face-to face questionnaire interview to investigate the information of mercury exposure and risk factors of dementia. The concentration of blood mercury was measured by cold vapor atomic absorption spectrophotometry. The results showed that blood mercury level did not be different between dementia patients (8.65±5.46 μg/L) and control subjects (8.90±4.07 μg/L) (P = 0.1535). After adjusting for age and gender, participants with higher education levels, regular exercise habits had significantly protective risk of dementia than controls. However, people had diabetes mellitus, or heart diseases had significantly increased risk of dementia than controls. In addition, we found significantly positive correlations between blood mercury and intake frequency of large-sized remote sea fish, shrimp, crab, and fish ball in total subjects. Given the limitation of small sample size in our study, the continuous surveillance and survey on patient's blood mercury might be necessary in future.

THE ASSOCIATION BETWEEN URINARY HEAVY METALS AND THE RISK OF MILD DEMENTIA IN THE COMMUNITY-BASED SCREENING PROGRAM

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Background : The percentage of the elder adults(age≧65 years old) and aging index in Taiwan were 12% and 85.7% in 2014. The incidence of dementia was more public attention. Ascertainment of dementia 8 (AD8) is a brief informant interview used to detect very mild dementia in the community-based screening program. The aim of this study is to explore the association between AD8 abnormality and urinary heavy metal concentrations in elder population.

Methods : This study enrolled all participants from the community-based integrated screening samples in 3 townships, Chiayi Country, Taiwan. Of the 1010 elder people with complete information from the questionnaires, 878 received the examination of AD8 and had levels of urinary heavy metals. A questionnaire was administered to study participants, collecting information on demographics, life habits, and AD8 score. AD8 abnormality was identified in those with AD8 score is≧2. We measured the urinary levels of arsenic, cadmium, chromium, nickel and lead by using inductively coupled plasma mass spectrometry. Multivariate logistic regression and 95% confidence intervals were applied to estimate the risk of AD8 abnormality and potential effects of AD8 abnormality -related risk factors.

Results : Female and less physical activity had significantly increased risk of AD8 abnormality, after adjusting for gender, age and township (all $p < 0.05$). Higher levels of urinary lead (Pb) were observed in the people with AD8 abnormality than those with AD8 normality. In addition, female also had higher

levels of urinary Pb than males. After adjusting for all risk factors, female and urinary Pb were independently risk factors for AD8 abnormality.

Conclusions: Female and increased levels of urinary Pb were independent risk factors. In addition, people with current physical activity had protected risks of AD8 abnormality in Taiwanese. Community-based multiple screening for mild dementia through AD8 examination was an applicative tool to explore the related risk factors of mild dementia.

NO MAN IS AN ISLAND: A GROUNDED THEORY STUDY OF PET ATTACHMENT SUPPORT AMONG OLDER PERSONS IN PHILIPPINE COMMUNITY SETTINGS

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ABSTRACT
Background: Dependency among older persons triggers them to seek out attachment and social support. Accordingly, pets have been considered as attachment figures. However, much of existing literature focuses on the impact of pet ownership, while the process behind pet attachment support among older persons remains a blankspot.

Aim: The overall intent of the study is to develop a model to describe the process by which pet attachment support is experienced among a selected group of older persons in Philippine community settings.

Methods: Strauss and Corbin's Grounded Theory design was used. A total of 20 older persons in various Philippine community settings in National Capital Region (NCR) and in Central Luzon (Region 3) were purposively selected to participate in semi-structured interviews. Field texts were subjected to thematic analysis involving open, axial and selective coding. Finally, truthfulness and validity of the findings was ensured through member checking procedure.

Findings: The study generated The Inosculation Model of Pet Attachment Support. It comprises of three phases relative to pet attachment support, namely: Initiating, Intertwining and Interlocking. The initiating phase is characterized by the need for support and security that triggers the dependent older persons being around with the pet. The intertwining phase is characterized by the older person not just accepting the responsibility on taking care of pet but also motivating them to become fully independent individual in being with the pet. Lastly, the older persons' continuous engagement through the aforementioned bonding activities further stabilized and deepened the pet-owner relationship as being one with the pet brings them to interlocking phase.

Conclusion: This study afforded a theoretical model with a view to contributing to the development of structured and optimized delivery of pet therapy as an intervention.

Keywords: Philippines, older person, grounded theory, pet attachment support.

SOLUBLE MILK PROTEIN SUPPLEMENTATION ASSOCIATED WITH MODERATE PHYSICAL ACTIVITY IMPROVES MUSCLE FORCE AND LOCOMOTION IN AGED RATS.

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CONTEXT AND OBJECTIVES
Loss of muscle mass and function, called sarcopenia, occurs with aging. Adequate protein intake and physical activity are considered as two crucial interventions to maintain both muscle mass and functionality in elderly subjects. The aim of this study was to investigate the impact of a protein supplementation with different milk proteins, associated with a moderate exercise, on muscle and locomotor functions in aged rats.

METHODS
We investigated the effect of 8-week supplementation with different milk proteins, such as caseins (CAS), whey (WH) or soluble milk proteins (PRO), on muscle force and gait analysis in trained aged rats Wistar RjHan (17 month-old, n=8/group). Animals followed moderate intensity protocol training with running exercises on treadmill at maximum speed 10 meters/min, during maximum 30 min/day, 5 days/week for 8 weeks. Just after treadmill exercise, a bolus of 0.85 g of CAS, WH or PRO was given in order to increase by 20% the protein content of the diet. Muscle force was evaluated using the grip test (Bioseb) and locomotor activity was measured in an open-field (Actimeter, Bioseb). Furthermore, an extensive gait analysis was performed using the Gait-Lab system (Gait-Lab, View Point) which is a highly sensitive tool recording the rat's footprints on a glass plate to assess gait and locomotion.

RESULTS
After 8 weeks, grip strength (expressed in g/mg of muscle mass) was significantly higher in rats from the PRO group than in CAS and WH groups. Also, locomotor parameters measured in the open-field, such as distance travelled, activity time and maximum speed, were higher in the PRO group than in CAS and WH groups, without any difference between CAS and WH groups. Gait analysis using the Gait Lab system showed a training-induced increase in voluntary gait speed after 8 weeks in the 3 groups, which was significantly higher in the PRO group. Also, a training-induced increase in stride frequency was observed and was higher in the PRO group.

CONCLUSION
In aged rats, a supplementation with soluble milk proteins after a moderate exercise is an effective way to improve muscle force and locomotor activity. These results suggest that soluble milk proteins consumed just after a moderate exercise could be more beneficial than whey. Therefore, soluble milk proteins could be considered as an interesting nutritional strategy in combination with physical activity to counteract the effect of sarcopenia in the elderly.

HERBAL TONIC TO IMPROVE DEMENTIA

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ABSTRACT
With ageing population, dementia has become a global problem. The two major causes of dementia are Alzheimer's disease and cerebrovascular disease. Despite intensive research, the drug treatment for dementia has limited efficacy. A number of Chinese herbs and herbal formulae have been used for dementia symptoms such as loss of memory, cognitive impairment, seizures and tremors. Some herbs are also found to be beneficial to vascular health.

The aim of the current study was to evaluate a herbal formula which is proposed to have protective effects against neuro-degeneration and vascular dementia at the same time. In vitro and in vivo research platforms were applied to identify the mechanism of action of the selected herbs in support of neuro-regeneration.

Our preliminary results indicated that our TG formula (0.25-1 mg/ml) being developed (containing Gastrodiae Rhizoma, Uncariae Ramulus cum Uncis, Chuanxiong Rhizoma, Polygalae Radix, and

Puerariae Lobatae Radix) attenuated vascular dementia in oxygen-glucose-deprived PC12 cells in vitro, as detected by MTT assay; TG Formula at 1.29 and 2.6 g/kg attenuated MCAO (middle cerebral artery occlusion)-induced brain infarct and neurological score in rats in vivo. Further study on the underlying mechanisms will be performed. Moreover, this formula (0.125-1 mg/ml) attenuated the toxicity of beta-amyloid in PC12 cells in vitro using MTT assay; It (0.5-1 mg/ml) also decreased beta-amyloid-induced late apoptosis as measured by Annexin V-PI double staining. Moreover, it (0.25-1 mg/ml) also inhibited acetylcholinesterase activity. The beneficial effect and the underlying mechanisms of this formula on Alzheimer's disease will also be investigated both in cells and mouse model (5xFAD Alzheimer's disease model).

In summary, our TG formula has been found its potential in attenuating vascular dementia. Based on the in vitro data for Alzheimer's disease, this formula also showed protection against beta-amyloid. Therefore, this formula may serve as a health supplement to improve vascular dementia and Alzheimer's disease in clinical setting.

THE IN VIVO AND IN VITRO NEUROPROTECTIVE EFFECTS OF INNOVATIVE CHINESE MEDICINE FORMULA AGAINST DEMENTIA

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Abstract:
Health burden raising from ageing is becoming apparent in last few decades. Currently, ageing-related neurodegenerative diseases such as Alzheimer's disease (AD) and vascular dementia are the two most common types of dementia. They are incurable but the emerged symptoms can only be slowed down [1]. The currently used drugs on dementia aim to regulate neurotransmitters. However, these medications are not targeting on the pathological processes of dementia including oxidation [2] and β-amyloid cascade [3], etc. The chemical components and organic extracts of Traditional Chinese Medicines (TCM) such as Tianma (TM) and Danshen (DS) have been reported to have neuroprotective effects. However, the effects of these water extract are not well-studied.

Based on previous works on single herb water extract and different concentration ratio of DS and TM, we have selected DS and TM in the ratio of 2:1 and this combination was named as DT formula. The objective of our study was to investigate the neuroprotective effects of DT formula using in vivo middle cerebral artery occlusion (MCAO) rat model to mimic the ischemic stroke condition, which is the major cause of vascular dementia. Besides, we also studied the effect of DT formula against AD using 5xFAD transgenic mice model. The underlying mechanisms were further investigated using various in vitro platforms including oxygen-glucose deprivation/reperfusion model (OGD/R), β-amyloid induced cell death and inhibition of acetylcholinesterase activity.

The SD rats were subjected to MCAO for 2 hours and followed by 24 hours reperfusion. The treatments were orally administered 1 hour before the MCAO. Our results demonstrated that low dose (1.067 g/kg) and high dose (2.134 g/kg) DT formula could significantly ameliorate the neurological deficit of MCAO-operated rats from 2.58 to 1.91 ($p<0.05$) and 1 ($p<0.001$), respectively. The brain infarct volume was significantly decreased from 0.42 cm3 to 0.21 cm3 ($p<0.01$) and 0.13 cm3 ($p<0.001$) after oral administration of low dose and high dose of DT, respectively. The activities of anti-oxidative enzymes (glutathione peroxidase and superoxide dismutase) in MCAO-operated rats were enhanced significantly ($p<0.05$) by DT formula. The anti-inflammatory effects of DT formula was revealed by the significant inhibition of inflammatory cytokines (TNF-α and IL-6) production after MCAO. Besides, we also studied

the neuroprotective effects of DT formula using 5xFAD transgenic Alzheimer's disease mice. The treatment was started with the 4 months old mice by oral administration and lasted for 8 weeks. The learning ability and spatial memory of the mice were assessed using Morris Water Maze (MWM). From the MWM, the preliminary results showed that 2.1 g/kg and 4.2 g/kg of DT treatment on 5xFAD would improve the performance in platform searching (i.e. lower latency) during the acquisition training and more island entries when compared with the control group during the probe test. We further elucidated the neuroprotective mechanisms of DT formula using OGD/R on PC12 cell line for vascular dementia. We also studied β-amyloid induced toxicity as well as the inhibitory effects of DT formula on acetylcholinesterase activity on PC12 cell line. DT formula was found to ameliorate β-amyloid-induced cell death from 42% to 61% ($p<0.001$). Our results also demonstrated that DT formula at 500 μg/ml showed the most significant attenuation of β-amyloid-induced toxicity on PC12 cells by 21% ($p<0.001$) and also inhibited acetylcholinesterase activity by 26% ($p<0.001$).

The neuroprotective effect of DT formula towards cerebral ischemia and reperfusion damage was demonstrated using the in vivo MCAO rat model and in vitro OGD/R model. These findings suggested that DT formula may protect neuronal cell death due to cerebral ischemia and reperfusion injury, which may consequently lead to vascular dementia. β-amyloid deposition and cholinergic deficit are major pathological events in AD. The results from in vitro studies provided the evidence of using DT formula to tackle this situation. Furthermore, the preliminary result from in vivo MWM also revealed that the DT formula may provide a modulatory effect in Alzheimer's disease.

In conclusion, we are the first group investigating the effects of DS and TM water extracts towards dementia. Our study also provided the first scientific evidence showing DT formula having anti-oxidative, anti-inflammatory, anti-β-amyloid-induced toxicity as well as the inhibitory effects on acetylcholinesterase activity. All these effects accounts for the neuroprotection against cerebral ischemia and reperfusion induced vascular dementia in the MCAO rat model as well as the 5xFAD AD mice model. Our results suggested the potential use of this innovative formula as a herbal supplement for elderly with dementia.

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FORMULATION OF CHINESE MEDICINES TACKLING DEMENTIA AND OSTEOPOROSIS

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Abstract:
Health burden raising from ageing is becoming apparent in last few decades. Currently, ageing-related degenerative diseases such as dementia (Alzheimer's Disease (AD) and vascular dementia (VaD)) and osteoporosis (OP) are incurable but the emerge of the symptoms can only be slowed down [1, 2]. It has been reported that there are clinical association in these two diseases, but current medication is usually single-targeting. The chemical components and organic extracts of Traditional Chinese Medicines (TCM) such as Tianma (TM) and Danshen (DS) have been reported to have neuroprotective and Nuzhenzi

(NZZ) for osteoprotection. However, the effects of these water extract are not well-studied. Our group hypothesized that this innovative formula could provide neuroprotection towards dementia, meanwhile promote bone health.

The reduced activities of anti-oxidative enzyme were reported in the AD, VaD and OP. This would eventually lead to the accumulation of reactive oxygen species and tissue damaged as consequence. Therefore the anti-oxidative effect of the three single herb was studied by employing H2O2-induced oxidative injury on PC12 cells and UMR-106 cells for neuro- and osteo-protection, respectively. 125 μg/ml DS, 1000 μg/ml TM and 125 μg/ml NZZ could significantly ($p < 0.001$) rescue the PC12 cell survival from 47.6% to 72.5%, 75.0% and 63.7%, respectively. Significant ($p < 0.001$) anti-oxidative effects of these 3 herbs was also revealed in the UMR-106 cells. 250 μg/ml DS, 1000 μg/ml TM and 125 μg/ml NZZ could ameliorate the cell survivals by 19.0%, 19.1% and 17.2%, respectively. We further investigated the neuroprotective effect of single herbs on β-amyloid (Aβ)-induced cell death on PC12 cells. Significant increase ($p < 0.001$) in cell survivals were observed when 1000 μg/ml DS, 1000 μg/ml TM and 250 μg/ml NZZ were used individually.

The above findings allow us to further determine the concentration ratio among the three herbs. As neuroprotection is our major aim, we combined the concentration ratio of DS and TM at 4:1, 3:1, 2:1, 1:1, 1:2, 1:3 and 1:4. The effects of the formula was first investigated using Aβ-induced cell death on PC12 cells. The ratio of DS:TM at 2:1 could provide the highest enhancement on cell survival by 25% significantly ($p < 0.001$). Based on this result, we further investigated the osteoprotective effect of the formula with the addition of NZZ, by the concentration ratio of DS:TM:NZZ at 2:1:0, 2:1:1, 2:1:2, 2:1:3. The β-glycerophosphate and Vitamin C induced Calcium deposition on UMR 106-01 cells assay was employed. The Calcium deposition was significantly ($p < 0.001$) increased by these 4 formulae. We are also interested in whether the addition of NZZ would enhance the effect of neuroprotection in the Aβ-induced cell death on PC12 cells. However, cytotoxicity was potentiated when NZZ was included. Therefore, the innovative formula of DS to TM at concentration ratio of 2:1 was determined for our further studies.

In conclusion, we are the first group investigating the single herb effects of DS, TM and NZZ water extracts towards dementia and OP. Our study also provided the first scientific evidence showing these water extracts having anti-oxidative, anti-β-amyloid-induced toxicity as well as the elevation on calcium deposition. These results allow us to further study the combined use of DS and TM formula for neuro- and osteo-protection, as well as exploring the potential use of this innovative formula as a herbal supplement for elderly with dementia and OP.

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PREVALENCE OF MAJOR COMPONENTS OF GERIATRIC SYNDROMES AND THEIR ASSOICATION AMONG NURSING HOME RESIDENTS IN AL-MEDINA-KSA

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BACKGROUND:
By the end of 2050, people who aged 60 or more in KSA will be 25 % of total population, 40 million1. Thus, there will be more than 10 million people aged 60 or more by 2050.

OBJECTIVE:
Prevalence of major components of geriatric syndromes among nursing home residents in Al-Medina-KSA. Finding its relation to the demographic data to be able to modify it.

DESIGN
Cross-sectional study

PARTICIPANTS:
A total of 75 elderly (51 male, 24 female) is screened in the Medina Nursing Home after take the permission.

MAIN MEASURES:
An in-person interview is done by the researchers to answer the questionnaires; no self-answer is done as the majority is illiterate. Each questionnaires was taking about 35 minute per participate. Questionnaires was divided into two part, part one contain Demographics factors (Demographics included age, gender, occupation, marital status, number of offspring, education, Smoker, and Chronic diseases.) and part two contain Geriatric syndromes (functional decline, Cognition and Incontinence).

RESULTS:
1-Sample and Demographic factors:
A total of 75 participates of the same nursing home were screened. Mean age was in the range of 80-89 years. 87 % of the participates was originally from Madinah. Majority of subjects had no jobs. 75% of the participates (56) are single and only 6.3 % are married. On other hand those married (75%) have no offspring. Illiterate was the dominant educational sate by 90.7% (68 persons). Smoker percentage was only 18.7% (14 persons) where those Ex-smokers are 14.7%. Most of the participates have chronic disease, diabetes mellitus was the highest among them by 48%. shows the demographic factors details.

2-Geriatric Syndromes:
In the category of functional status (function decline), totally dependent (<1 ADL) is 19% of the subject, totally independent is 31 %(=6ADL) where those partially dependent is 51 %.(≥1ADL). 96% of the subjects have Mini Mental State Examination (MMSE) score below 17. Urinary incontinence was reported by 9% of subjects (≥1ICIQ-UI Short Form).

CONCLUSIONS:
Major component of geriatric syndromes were found to be very high among nursing home residents in Medina. Score of mini–mental state examination (MMSE) was globally very low, diabetes mellitus was the commonest among the chronic disease. However urinary incontinence and inactivity was not very prominent. Further studies are recommended to explore the rest of factors and minimize it.

CHARACTERIZATION OF THE GUT-ASSOCIATED LYMPHOID TISSUE IN SAMP8 MICE

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Aging is characterized by an increase of the susceptibility to some diseases that involve the immune system. In the intestine, the gut associated lymphoid tissue (GALT) has an important role in the protection of the host in front of pathogens. The aim of this study was to characterize the GALT at different stages of the development in a model of senescent mice. Mice prone (SAMP8 strain) and resistant (SAMR1 strain) to accelerated senescence were used. The ages chosen for the study were 3 weeks and 2, 6 and 9 months. Mesenteric lymphoid nodes (MLN) and Peyer's patches (PP) of the small intestine were obtained and lymphocyte populations were analyzed. In both strains, cell counts increased with age in both MLN and PP ($p < 0.05$), though the rate in SAMP8 was lower. In SAMP8, the percentage of activated Th lymphocytes increased with age in both tissues ($p < 0.05$). At 9 months, SAMP8 mice showed a 1.8-fold increase in activated Th lymphocytes in MLN (no change in SAMR1) while in PP the increase in activated Th lymphocytes was only observed in SAMR1 mice (1.6-fold). Since the Treg population showed little changes with aging, the T activated/Treg ratio was increased with aging in both tissues ($p < 0.05$), especially in SAMP8 mice. Results indicate that the degree of GALT basal activation increases with age and that aged SAMP8 mice may have a reduced mucosal immune response (immunosenescence). This condition might explain the higher susceptibility to infections and pathologies associated to aging.

THE INTESTINAL IMMUNE RESPONSE TO STAPHYLOCOCCUS AUREUS ENTEROTOXIN B IS COMPROMISED IN SENESCENT MICE.

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Aging is characterized by a progressive decline in the immune function that increases the susceptibility to some diseases. Staphylococcus aureus enterotoxin B (SEB) is a superantigen that induces, as previously shown in young rats and mice, a massive activation of T helper lymphocytes which results in a significant stimulation of the gut-associated lymphoid tissue (GALT). The aim of this work was to analyse the GALT response in senescent mice after a SEB challenge. Experiments were performed in 2 month-old (young) and 6 month-old (senescent) SAMP8 mice, that were administered intraperitoneally with 25 µg of SEB. Twenty-four hours after the challenge, mice were killed and samples of mesenteric lymphoid nodes (MLN), Peyer's patches (PP) and segments of the jejunum mucosa were obtained. In young mice, SEB increased the percentage of activated T helper lymphocytes in MLN and PP and stimulated the intestinal expression of TNFα and IL-10 (all, $p < 0.05$). However, the senescent mice were not able to respond to the SEB challenge. Control senescent mice showed an increase in some inflammatory markers such as cell recruitment in MLN and TNFα expression in the intestinal mucosa (both $p<0.05$), compared to young mice. These results indicate that senescent mice have an impaired mucosal immune response characterized by a basal proinflammatory state (inflammaging) at intestinal level, and a weak specific immune response when exposed to a pathogenic antigen.

OXIDATIVE STRESS-INDUCED p66 EXPRESSION: KEY MECHANISM OF AGE-RELATED COCHLEAR SENSORY HAIR CELL LOSS

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Background and Introduction: In our aging society, age-related hearing loss or presbycusis is increasingly important. Based on observations of temporal bones from patients with presbycusis, Schuknecht (Schuknecht and Gacek, 1993) proposed the classification into three major forms, namely sensory, neural, and strial presbycusis according to the location of damage (sensory epithelium, spiral ganglion neuron, or stria vascularis). To date, the mechanisms underlying the age-related hearing loss remain unclear. Based on our previous study (Menardo et al., 2013) showing that the premature age-related hearing loss observed in senescence-accelerated mouse prone 8 (SAMP8) mice was correlated with altered levels of anti-oxidant enzymes and decreased activity of mitochondrial functions, we hypothesis that the oxidative stress may play a key role in presbycusis.

Methods: To investigate the contribution of the oxidative stress in presbycusis, we exposed the p3 mouse cochlear explants to hydrogen peroxide (H2O2) in vitro. The cochlear cell senescence or degeneration was evaluated using the specific biomarkers. In addition, the role of endogenously-produced ROS in age-related hearing loss was assessed in adult p66KO mice which have a decreased ROS production.

Results: Our results provide the evidence that the oxidative stress plays a key role in age-related hearing loss and cochlear sensory hair cell apoptosis. We demonstrate that H2O2 exposure induced a premature occurrence of cochlear sensory hair cell senescence and apoptosis, illustrated by the massive increase of the cell senescence and apoptosis biomarkers such as SA-beta gal□□□□H2AX, Annexin V and TUNEL, mainly in the cochlear sensory hair cells, but not in the spiral ganglion neurons. Interestingly, our in vivo results from p66 KO and WT mice provided the functional and morphological evidence that the

targeting of oxidative stress by genetic interventions protect the cochleae against age-related sensory hair cell death and hearing loss.

Conclusion: Our results suggest that oxidative stress plays crucial role in age-related cochlear sensory hair cell degeneration and hearing loss. The use of anti-oxidants may be an attractive therapy to slowdown or stop the sensory presbycusis.

GENDER RELATED DIFFERENCES IN FUNCTIONAL CONNECTIVITY AND ITS ALTERATIONS DURING NORMAL AGING: INFLUENCE OF APOLIPOPROTEIN E GENOTYPE

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The normal brain undergoes a substantial decrease of functional connections within resting-state networks during aging, but gender-related differences in functional connectivity remain largely unknown. The ε4 allele of the apolipoprotein E gene (ApoE) is well established risk factor for Alzheimer's disease (AD). The ApoE effect on AD risk is stronger in women than in men, but its mechanism is not completely understood. The aim of this study was to determine the possible gender-related differences of the alterations of brain functional connectivity in normal aging and to define the effect of ApoE genotype on theses alterations. We examined age-related differences in resting state functional connectivity assessed by interhemispheric EEG coherence in 141 non-demented volunteers (age range 20-80 years), subdivided into subgroups of those younger and older than 50 years of age and stratified by gender and ApoE genotype. All subjects were free of neurological or psychiatric conditions and underwent cognitive screening.
The results showed gender-related differences in resting state functional connectivity with women demonstrating greater interhemispheric coherence in younger age and higher coherence reduction during aging. The most prominent disruption of functional connectivity was found in the older female ApoE ε4 carriers.. The reduction of interhemispheric coherence of alpha activity in elderly subjects correlated with the worse performance in verbal memory test. The progressive decline in interhemispheric connectivity contributes to memory decrement and suggests the impact of age-related disconnection process in pathogenesis of AD in women carrying ApoE ε4 allele.
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DIET QUALITY IN LATER LIFE: THE IMPORTANCE OF SOCIAL FACTORS

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Background: Poor nutrition is common in older people, but little is known about influences on food choice at this age or the most effective strategies to promote diet quality in older age. Recent studies in the US have highlighted the role of 'resilience' and the role of psychosocial factors that may mediate the effects of background characteristics, such as illness or disadvantage, on diet. To date, very few UK studies have examined the links between psychosocial factors and diet in older age. The aim of the

present study was to examine social influences and their cross-sectional relationships with diet quality in a UK cohort of older community-dwelling men and women.

Methods: Between 1998 and 2003, the diets of 1677 men and 1540 women aged 59-73 years, taking part in the Hertfordshire Cohort Study, were assessed by administered food frequency questionnaire. A prudent diet score, derived from a principal component analysis of the dietary data, was calculated for each participant and was used as an indicator of diet quality. High scores indicated frequent consumption of fruit, vegetables, wholegrain cereals and oily fish. A social health questionnaire undertaken by 1048 of the men and 862 of the women assessed a range of psychosocial factors including social support, social network, participation in social and cognitive leisure activities, and control at home.

Results: Mean (SD) prudent diet score was significantly lower in men -0.328 (1.224) than in women 0.358 (1.110). In both men and women, diet quality was positively related to social support; specifically, greater confiding/emotional support was associated with a higher prudent diet score [(0.006; 95% CI 0.002, 0.010; p=0.001 for men); (0.005; 95% CI 0.000, 0.009; p=0.029 for women)]. In men but not in women, greater practical support was also associated with a higher diet score (0.004; 95% CI 0.001, 0.006; p=0.010). In contrast, a large social network and feeling close to many people were both associated with higher prudent diet scores (0.006; 95% CI 0.001, 0.010; p=0.010) in women, but not in men. For both men and women, higher overall participation in leisure activities was related to higher prudent diet score [(0.022; 95% CI 0.017, 0.028; p<0.001 for men); (0.018; 95% CI 0.012, 0.024; p<0.001 for women)]; furthermore, increased participation in activities of a more cognitive nature [(0.020; 95% CI 0.015, 0.024; p<0.001 for men); (0.016; 95% CI 0.011, 0.022; p<0.001 for women)], as well as in activities of a more social nature [(0.010; 95% CI 0.006, 0.015; p<0.001 for men); (0.010; 95%CI 0.005, 0.015; p<0.001 for women)] were both associated with a higher prudent diet score. These associations were robust to adjustment for social class, age left education and number of comorbidities. Diet score was not related to control at home.

Conclusions: In community-dwelling older adults, a range of social factors that include increased social support, a large social network, and increased participation in social and cognitive leisure activities, are associated with better quality diet. Understanding how social factors influence diet in later life will be important for the development of interventions to promote diet quality in older people.

CARBAMYLATION, A NONENZYMATIC POST-TRANSLATIONAL MODIFICATION OF PROTEINS ASSOCIATED WITH LONGEVITY

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Ageing is associated with tissue alterations, which may be explained by nonenzymatic post-translational modifications (e.g. glycation, oxidation, carbamylation) of proteins. Some pathological contexts like diabetes, vascular diseases or renal failure are known for amplifying these chemical modifications. A still poorly investigated reaction is carbamylation, which corresponds to the binding of isocyanic acid, a urea by-product, to protein amino groups. This process leads to the formation of carbamylation-derived products (CDPs) including homocitrulline (HCit), which results from lysine carbamylation. In vitro experiments have shown that carbamylation contributes to the alteration of structural and functional properties of proteins. However, the metabolic fate of carbamylated proteins in vivo is still unclear, especially during ageing. In this study, we have evaluated the tissue accumulation of CDPs over the time in three mammalian species. We have observed that HCit concentrations progressively increased in murine tissues from birth to 2 years, the highest content being noted in skin. The same evolution was observed in bovine and human skin, with an elevation of 11.5 and 8.1-fold between the young and old subjects, respectively. Interestingly, this reaction impacts more intensely matrix proteins, probably because of their long half-life. Indeed, skin type I collagen and elastin were significantly carbamylated in oldest subjects compared to youngest ones. These results showed that carbamylation is a physiological

reaction associated with ageing, which leads to an accumulation of CDPs in tissues. Such modifications could induce turnover alterations and cellular dysfunctions contributing to age-related complications.

MESENCEPHALIC ASTROCYTE-DERIVED NEUROTROPHIC FACTOR MAINTAINS ENDOPLASMIC RETICULUM HOMEOSTASIS IN C. ELEGANS

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Mesencephalic Astrocyte-derived Neurotrophic Factor (MANF) has been recently recognized as the promising therapeutic target for the treatment of the Parkinson's disease as it exhibits remarkable neurotrophic activity promoting survival of the dopaminergic neurons, yet with unknown molecular mechanism. We aim to identify novel components of the MANF signaling transduction pathway. We take advantage of the powerful genetics of the model organism Caenorhabditis elegans and utilize our new CARGIS (CRISPR-Cas-9 and RNA-seq-based Genetic Interactor Screen) strategy starting from generation of the manf knock-out by CRISPR, identification of differentially regulated genes by RNA-seq, construction of GFP reporters for mutagenesis and RNAi screen, to the discovery of the genetic interactors and molecular pathway in which the manf gene functions. C. elegans carrying two independent manf deletion alleles tm3603 or dma6 are viable and superficially wildtype in contrast to fly, fish or rodent models, nonetheless have several genes differently regulated including hsp-4, a target of the untranslated protein response (UPR). We have crossed tm3603 allele with zcIs4(hsp-4p::GFP) allele and observed markedly enhanced GFP fluorescence in the intestinal and hypodermal cells compared to wild-type manf allele. We determined that manf mutants induce UPR by IRE-1, RTCB-1 and XBP-1 activities. Moreover we isolated two novel suppressor mutations of the induced UPR which await for the mapping analysis. We demonstrate that the deletion of the manf gene is not lethal even though leads to endoplasmic reticulum stress in C. elegans. Our preliminary data promise identification of new regulators and ascertain the mechanisms of the MANF signaling pathway that should provide novel targets to treat Parkinson's disease and other diseases associated with aging.
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THE IMPACT OF EDUCATION ON CEREBRAL AND CARDIOVASCULAR CHARACTERISTICS OF PATIENTS WITH VASCULAR ENCEPHALOPATHY

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Background: Interesting problem is why does education play such a big role in longevity (Smith, 2012)? We studied the impact of education on the development of chronic cerebrovascular disease associated with mild cognitive impairment. Aim: to investigate the cerebrovascular ultrasound and neurophysiologic characteristics of patients with vascular encephalopathy (VE) with different levels of education in resting state and during cognitive tests.

Methods: Seventy-seven female patients with VE (age range 60-80 years) were examined. All patients were divided into two groups: with secondary education (A) and with tertiary education (B). Patients performed cognitive tests: verbal fluency test (VFT), Luria's verbal memory test and the 7 serial subtraction test (100-7). Blood pressure and heart rate were evaluated before and after cognitive tests. Duplex scanning of main arteries of the head and the DC potentials in different areas of head were performed. A and B groups did not differ in age. One-way ANOVA was used to determine differences between A and B group characteristics (Statistica-7).

Results: The subjects of the B group performed better 7 subtraction test in comparison with the A group ($F=4.2$, $p<0.05$). The heart rate reactivity during the performance of VFT was higher in the B group than in A group ($F=8.7$, $p=0.004$). Linear velocity of blood flow of the left internal carotid artery was higher in the B group than in A one after the Luria's test performance ($F=4.3$, $p<0.05$). The DC potentials in the frontal region were higher in the subjects of group B ($F=6.1$, $p=0.02$) during cognitive tests performance.

Discussion: The results show that the patients with higher education had certain advantages in performing cognitive tests and probably better blood supply in the left hemisphere during the tests. It is possible that not only the level of education influenced the neurophysiological and vascular differences, but also the subsequent professional activity could affect these distinctions.

Conclusion: VE patients with secondary and tertiary education had different cognitive abilities associated with different characteristics of cerebral blood flow.

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CHARACTERISTICS AND OUTCOMES OF PATIENTS OLDEST OLD ADMITTED TO A PRIVATE HOSPITAL

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The increase in life expectancy is a worldwide phenomenon, and the age group with the fastest growth is the group including individuals who are 80 years of age or older. In Brazil, while the average yearly geometric growth rate of the general elderly population (≥ 60 years) is approximately 3.3%, the rate among the oldest segment of that group is 5.4%, one of the world's highest. In the aging process, it has increased demand for costly health interventions. This study intends to describe and analyze the epidemiological profile of oldest old patients (≥ 85 years) admitted to the Hospital Albert Einstein.

Method This is a retrospective cross-sectional study. The study was conducted in Hospital Albert Einstein, located in Sao Paulo, Brazil. Population were oldest old patients (≥ 85 years) hospitalized from 2008 to 2013.

Results The oldest old patients grows every year and represented in 2013, 4.3% of admissions. The demographic changes of the last few years demonstrate the aging trend and increased number of admissions of patients in this age group.. In all age groups the females and hospitalizations for clinical condition were more prevalent. The admissions for circulatory and respiratory causes were the most frequent, followed by neoplasm. The number of readmission was highest in the age groups 91-95 and 96-100 years, and the length of hospital stay and hospital mortality were higher in the age groups 96-100 and >100 years.

Conclusion It is essential that healthcare professionals and institutions an effective organization of health systems promote the oldest old suitable to their conditions, limitations and potential health care, so you can identify their real needs and thus better utilization of resource.