Mechanisms of Ageing and Development xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Mechanisms of Ageing and Development

journal homepage: www.elsevier.com/locate/mechagedev

Reprint of: Musculoskeletal system in the old age and the demand for healthy ageing biomarkers☆

Sebastiano Collino[a,*], François-Pierre Martin[a], Leonidas G. Karagounis[b], Marie Noelle Horcajada[b], Sofia Moco[c], Claudio Franceschi[d], Martin Kussmann[a,e,f], Elizabeth Offord[b]

[a] Nestlé Institute of Health Sciences, Molecular Biomarkers, EPFL Innovation park, 1015 Lausanne, Switzerland
[b] Nestlé Research Center, Nutrition and Health, Vers-chez-les-Blanc, CH-1000 Lausanne 26, Switzerland
[c] Nestlé Institute of Health Sciences, Natural Bioactives and Screening, EPFL Innovation park, 1015 Lausanne, Switzerland
[d] Interdepartmental Centre "L. Galvani" CIG, University of Bologna, Via Belmeloro 3, 40126 Bologna, Italy
[e] Faculty of Life Sciences, Ecole Polytechnique Fédérale Lausanne (EPFL), Lausanne, Switzerland
[f] Faculty of Science, Interdisciplinary NanoScience Center (iNANO), Aarhus University, Aarhus, Denmark

ARTICLE INFO

Article history:
Available online xxx

Keywords:
Ageing
Metabolomics
Bone
Muscle
Longevity

ABSTRACT

Population ageing has emerged as a major demographic trend worldwide due to improved health and longevity. This global ageing phenomenon will have a major impact on health-care systems worldwide due to increased morbidity and greater needs for hospitalization/institutionalization. As the ageing population increases worldwide, there is an increasing awareness not only of increased longevity but also of the importance of "healthy ageing" and "quality of life". Yet, the age related chronic inflammation is believed to be pathogenic with regards to its contribution to frailty and degenerative disorders. In particular, the frailty syndrome is increasingly being considered as a key risk indicator of adverse health outcomes. In addition, elderly may be also prone to be resistant to anabolic stimuli which is likely a key factor in the loss of skeletal muscle mass with ageing. Vital to understand these key biological processes is the development of biological markers, through system biology approaches, aiding at strategies for tailored therapeutic and personalized nutritional program. Overall aim is to prevent or attenuate decline of key physiological functions required to live an active, independent life. This review focus on core indicators of health and functions in older adults, where nutrition and tailored personalized programs could exhibit preventive roles, and where the aid of metabolomics technologies are increasingly displaying potential in revealing key molecular mechanisms/targets linked to specific ageing and/or healthy ageing processes.

1. Introduction

Ageing can commonly be characterized as a progressive, generalized impairment of biological functions resulting in an increased vulnerability to environmental challenge and a higher risk of disease and death (Kirkwood, 2005). Despite the enormous complexity of the ageing process, involving combinations of many biological and physiological variables, a small number of basic molecular mechanisms underpin the ageing process, involving a set of highly conserved mechanisms. One of the key mechanisms of the ageing process is the development of a chronic, low grade, inflammatory status named inflammageing and this condition has emerged as critical in the onset of the pathogenesis of major age-related chronic diseases (Fig. 1) such as atherosclerosis, type 2 diabetes, and neurodegeneration (Franceschi, 2007). Inflammageing plays a pivotal role in the most important geriatric conditions, such as sarcopenia, frailty, osteoporosis, and disability, thus contributing to elderly morbidity and mortality. Interestingly, a variety of tissue, organs (brain, liver), immune system contribute to the onset and progression of such a systemic inflammatory state. Musculoskeletal ageing is characterized by decline in bone (osteoporosis) and muscle mass and strength (sarcopenia),

☆ A publishers' error resulted in this article appearing in the wrong issue. The article is reprinted here for the reader's convenience and for the continuity of the special issue. For citation purposes, please use, the original publication details; Mechanisms of Ageing and Development, volume 134/11–12, November/December 2013, pages 541–547.

* Corresponding author. Tel.: +41 216326161.
E-mail address: sebastiano.collino@rd.nestle.com (S. Collino).

http://dx.doi.org/10.1016/j.mad.2014.03.002
0047-6374/

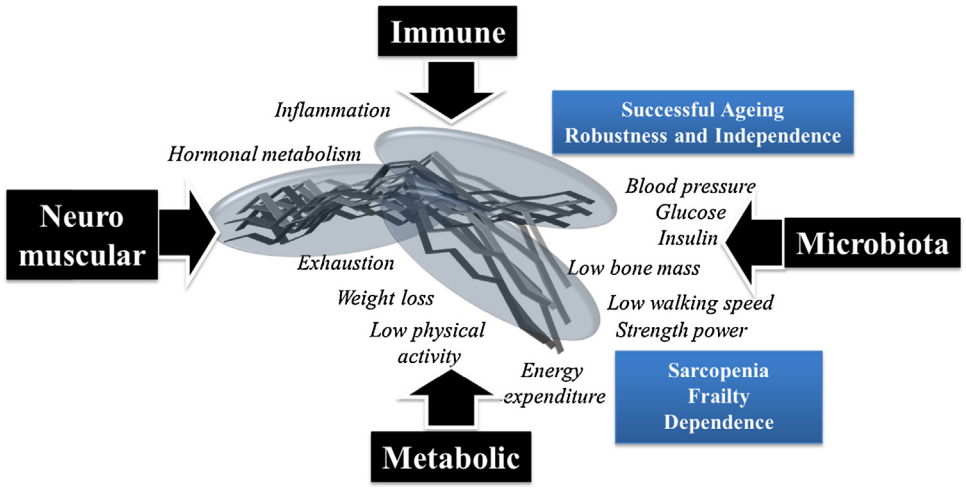

Fig. 1. System biology approaches together with the multifactorial origins of the age related disorders will help in characterizing different metabolic phenotypes among older adults.

increased joint pain and stiffness, reduced physical mobility, increased risk of falls and fractures. Physical functionality or mobility is a core indicator of healthy ageing in the elderly population (Milaneschi et al., 2010). Skeletal muscle loss is a major contributor to the frailty syndrome of ageing and can lead to reduced mobility and increased disability among older adults.

Metabolic phenotyping (metabolomics) offer a powerful new means for discovering molecular biomarkers and metabolic pathways that underlie disease risk. While the identification of biological markers of ageing is still on its infancy, their characterization is crucial in providing insights into mechanisms or strategies that can prevent or reverse the decline in certain of the affected networks and as such could extend health-span and prevent accelerated ageing.

Understanding the physiology of ageing is of tremendous importance to allow populations to grow old, disease-free and with a good quality of life. In this respect it is important to understand the natural ageing process and to elucidate where lifestyle and/or dietary interventions can have an impact (Heilbronn and Ravussin, 2005; Mair et al., 2005; Piper et al., 2005; Sinclair, 2005). The improvements in nutrition, sanitary conditions and medical care have led to a general increase in human longevity, with also plausible effects of the host–gut microbial metabolic interactions in health and disease (Tiihonen et al., 2010). Understanding the normal physiological process of ageing within the gut will contribute in managing the clinical and nutritional needs of the ageing populations. Indeed, there is nowadays increasing evidence that intestinal microbiota mediates crucial events towards the protection or degradation of health, influencing health ageing and maybe a key determinant of longevity (Biagi et al., 2013).

2. Physical functionality and nutrition in older adults

Skeletal muscle is the most abundant tissue in the human body and its plasticity is pivotal in maintaining optimal homeostatic regulation, metabolic health and physiological levels of functional capacity throughout life. Two triggers known to stimulate adaptations in skeletal muscle include contractile activity (weight loading and unloading) and nutrition (macro- and micro-nutrients). Repeated exposure to such stimuli over time initiate changes at the molecular level allowing skeletal muscle to adapt and alter its profile to meet the demands of its new environment. Under conditions of normal nutritional intake, this is to say when healthy individuals consume regular balanced meals whilst maintaining activities of everyday living, skeletal muscle protein mass remains essentially unchanged for lengthy periods of time. This maintenance of skeletal muscle mass is primarily due to the vacillation between the rates at which muscle (proteins) are synthesized and broken down, a process defined as net protein balance. In contrast, under conditions of immobility and reduced nutrient intake the rate at which muscle protein breakdown occurs is increased while simultaneously reducing the levels of muscle protein synthesis. This process may be exacerbated when combined with the normal process of ageing which also contributes to the loss of skeletal muscle mass. Specifically, between 20 and 80 years of age a 30% reduction in muscle mass accompanied by an almost 20% decline in cross sectional has been observed (Frontera et al., 2000). In the face of age related reductions in muscle mass and function it is paramount to maintain appropriate levels of nutrition and physical activity as means to attenuate such losses. Failure to do so may lead to weak muscles and subsequent impairments in mobility resulting in disability with loss of independent living. Collectively, these manifestations fall under the umbrella term of sarcopenia, the age-associated loss of muscle mass and function that is accompanied by loss of strength, contractile capacity and endurance (Fielding et al., 2011), although the precise mechanism(s) responsible for the sarcopenic phenotype remain to be elucidated.

Physical activity is a major determinant for improving muscle mass and function; however it is also well characterized that the appropriate nutrient intake may also play a pivotal role in muscle maintenance. In one of the first studies investigating the effect of a mixed meal on net protein balance in humans, it was reported that feeding a mixed meal was able to stimulate anabolism by stimulating muscle protein synthesis (Rennie et al., 1982) while simultaneously suppressing muscle protein breakdown (Yoshizawa et al., 1997) therefore switching net protein balance from negative (i.e. postabsorptive state) to positive (i.e. postprandial state) (Nagasawa et al., 1998). Increased amino acid availability is known to elicit increased rates of muscle protein synthesis (MPS) in both young (Greenhaff et al., 2008) and elderly individuals (Volpi et al., 2003) and this effect is amplified when combined with physical activity.

A major pathway involved in the regulation of muscle mass by nutrients (and contractile stimuli) is the AKT/mTOR/p70S6K signalling cascade (Schiaffino et al., 2013). The AKT pathway has been shown to be implicated in the regulation of both synthesis and breakdown processes. Activation of protein kinase B (PKB/c-Akt/Rac) has been shown to affect processes such as glucose utilization (Ueki et al., 1998) muscle atrophy (Sacheck et al., 2004),

Please cite this article in press as: Collino, S., et al., Reprint of: Musculoskeletal system in the old age and the demand for healthy ageing biomarkers. Mech. Ageing Dev. (2014), http://dx.doi.org/10.1016/j.mad.2014.03.002