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Review

Towards a biological geriatric assessment

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ABSTRACT

The aging process occurs gradually, is highly individual, with a high degree of inter and intra-individual differences. As such, within an aging population there is significant variation in regards to extent of age related disease and functional impairment. This variability between individuals is thought to be expressed as biological age. Currently, the comprehensive geriatric assessment (CGA), a multidimensional, interdisciplinary diagnostic process is used to determine an individual's medical, psychological and functional capability at older age. However, while the CGA utilises well-established markers of physical and functional parameters, it does not include any molecular measures that indicate an individual's biological age. Combining functional measures with molecular markers of biological age, could improve the current CGA by identifying individuals undergoing a rapid aging process. In this review, the current knowledge and clinical utility of potential biomarkers of aging are presented. Although no biomarkers indicative of biological age are currently being utilized in the clinical setting promising research advancements would suggest their application in the near future.

1. Introduction

Longevity coupled with deteriorating health has caused rising healthcare costs and an increased pressure on health systems to manage the growing number of older people. The high rates of institutionalization in the frail elderly lead to the development of the comprehensive geriatric assessment (CGA) (Pilotto et al., 2017). The CGA is a multidimensional, interdisciplinary diagnostic process that utilises subjective and objective measures to determine the medical, psychological and functional capabilities of older people (Pilotto et al., 2017). This approach has facilitated the development of a coordinated, integrated treatment plan that reduces morbidity and mortality in elderly populations (Pilotto et al., 2017). However, the CGA does not currently incorporate molecular biomarkers of aging. Molecular mechanisms that are causally associated to the aging process and age-related diseases may be indicative of physical decline, and provide unique insight into an individual's current and future health status.

The aging process occurs gradually and is an individual process with a high degree of inter and intra-individual differences (Belsky et al., 2017). For examples, some individuals with a chronological age of 85 years are physiological similar to chronologically younger individuals; while in others, physiological dysfunction may occur at a much younger age (60 years). Even in the case of identical twins, substantial differences in the timing of the onset of particular aging-associated symptoms are common (Fraga et al., 2005). Over the last decade the biological processes that contribute to aging and deteriorating health are being increasingly understood. In the seminal paper, López-Otín and colleagues describe 'The Hallmarks of Aging' consisting of nine overarching biological processes involved in aging in an attempt to provide a structural framework that defines biological aging (López-Otín et al., 2013). While these hallmarks may not be exhaustive of all the biological processes involved in aging, they do provide a framework around which a biological geriatric assessment (BGA) could be structured. A multidimensional BGA that couples molecular biomarkers with targeted intervention could not only identify individuals undergoing a rapid aging process but also allow for early, intervention and prevention of age-related diseases. A BGA would complement and enhance the current clinical CGA (Fig. 1). This targeted, individualized treatment approach based on the underlying biology has proven to be successful in the field of oncology, particularly in regards to tumor phenotyping (Bournet et al., 2016).

Biomarkers can be separated into two categories; biomarkers of exposure (risk of developing disease) and biomarkers of disease (diagnosis). In addition, a good clinical biomarker is usually determined by the following criteria: 1) the biomarker is reliable and sufficiently associated with the underlying disease process 2) it's clinically practical and 3) it guides clinical intervention (Bournet et al., 2016). However, despite these clear criteria, few attempts to isolate molecular markers of

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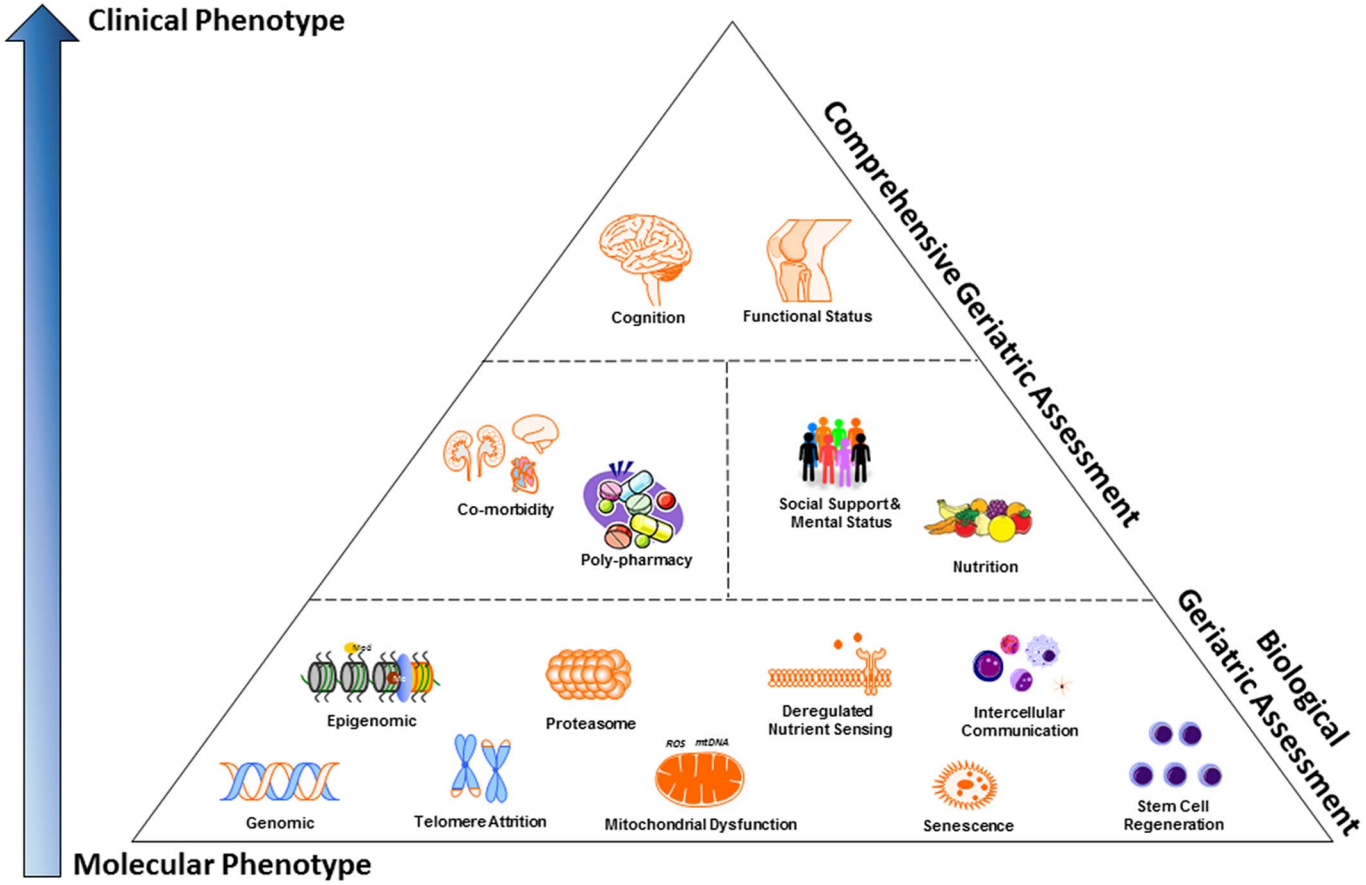

Fig. 1. A Biological Geriatric Assessment (BGA) will enhance the Comprehensive Geriatric Assessment (CGA)
A BGA could isolate individuals at risk of accelerated aging and allow for earlier clinical intervention and reduce functional.

aging (and associated diseases) have been undertaken. The few studies that have investigated these markers have shown promising results. For example, Mitnitski and colleagues assessed whether a biological frailty index outperformed a clinical deficits frailty index in predicting mortality of an aged cohort (Mitnitski et al., 2015). Interestingly, the combined use of both the biological and clinical index of frailty (AUC 0.75) outperformed the individual models (clinical AUC: 0.71, biological AUC: 0.66) for predicting mortality in an aged cohort (Mitnitski et al., 2015). Thus, there is an inherent need for large cohort studies that measure both clinical phenotype and molecular mechanisms to determine appropriate biomarkers of the aging process. Here we review the current evidence for the use of potential molecular biomarkers in a geriatric assessment with particular reference to the hallmarks of aging (López-Otín et al., 2013).

2. Aging

Social, environmental and biomedical influences in early years have a long-term impact on health and aging. Hence, age is considered a multi-dimensional concept that captures how people feel and function. However, defining the operational definition of aging has proven to be difficult with contentions over what factors should be included in this multi-dimensional process (Cosco et al., 2014). Operational definitions range from strictly biomedical, to strictly psychosocial highlighting life-satisfaction and well-being as the most essential components of successful aging. However, what is clear is that aging is a complex process requiring more than just survival as the outcome. The CGA combines most of the described constructs of aging (physiological, engagement, well-being, personal resources and extrinsic factors) in its multi-dimensional approach to treat and manage elderly patients. Thus, the BGA acting as a complement to this model similarly aligns with this definition of aging but with a strong focus on the physiological component.

3. Genomic instability

Current genomic techniques are approaching the point of being able to detect genetic variation in people with high accuracy and at a low cost. Given the ease of specimen attainment (blood) at first glance, genetic testing would appear to be the most useful biomarker for assessing an individual's rate of aging and physical decline. However, only a few genetic variants (*APOE* and *FOXO3A)* have been associated with longevity (Erikson et al., 2016; Broer et al., 2015; Fortney et al., 2015). Approaching the aging phenomenon from a different angle Erikson et al. demonstrated that healthy aging was associated with reduced genetic susceptibility to Alzheimer's and coronary artery diseases (CAD) (Erikson et al., 2016). Therefore, screening for the absence of genetic susceptibility for these diseases may identify groups of individuals with a slow aging process. In addition, it should be noted that there are documented differences in the rate of aging between populations (He et al., 2016), as such genetic markers of aging are likely to be ethnically diverse. In addition, aging is minimally heritable (~25%) even in environmentally homogenous populations (Christensen et al., 2006). Furthermore, any one polymorphism usually explains only 1–8% of an overall risk in a population and it is the additive effect of several such factors that increases overall risk of age-related disease by 20–70% (Ioannidis, 2003). Although there appears to be a greater genetic influence associated with centenarians (Milman and Barzilai, 2015). Identifying the differing clusters of genes within diverse ethnic populations that contribute to the rate of aging is essential to developing