Editorial

Ageing, Longevity, Exceptional Longevity and Related Genetic and Non Genetics Markers: Panel Statement

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In May 2012, a group of scientists and clinicians met in Athens (Greece) to consider the relevance of ageing, longevity, exceptional longevity and related genetic and non genetic markers. During this meeting, we firstly reviewed recent epidemiological and clinical studies on ageing, longevity and exceptional longevity, briefly analyzed the ageing theories and discussed successful and unsuccessful ageing also taking into account the evolutionary perspective. Secondly, we considered the three phenotypes based on the definition of ageing, longevity and exceptional longevity and the associated biomarkers. Third, we discussed proposed treatments suitable to counteract or slow down ageing. Finally, this panel produced a consensus statement to highlight the importance of ageing, longevity and exceptional longevity, since this is a rapidly increasing phenotype worldwide. We acknowledge that not all experts in this field may completely agree with this statement.

SUMMARY OF PANEL POSITION

1. Ageing is most likely one component of life, which first emerged in economically developed countries and results from a breakdown of self organizing system and reduced ability to adapt to the environment. Ageing processes are defined as those that amplify the vulnerability of subjects, as they become older, to the factors that finally lead to death. An emerging concept is the difference between chronological and biological ageing: tissues and organs of the same body may have a diverse rate of ageing in contrast with the chronological age of the individual, and conversely individuals with the same chronological age may have different rate of ageing and a different biological age.

2. Many variables contribute to ageing/longevity such as cultural, anthropological and socio-economic status as well sex and gender (women live longer than men) and ethnic differences (explained by discrepancies in healthcare, environmental and economic status, genetics as well as life occupation) also exist in relation to ageing/longevity, as well as stochastic events.

3. Successful ageing involves avoidance (or late onset) of age-related disease including cardiovascular disease which is the main cause of death, and other organ specific diseases, disability, preservation of desirable cognitive and physical function and social activities throughout the life span.

4. Many definitions of longevity are proposed, but at present no consensus definition has been established. On the basis of demographic data, we propose that exceptional longevity may be defined in relative and absolute terms. "Relative"

suggests that longevity is concept country/population specific and must take into consideration the life expectancy of the different populations/countries, which show great variability owing to historical, anthropological and socio-economic differences. In "absolute" terms longevity could be defined according to the maximum lifespan attained and scientifically validated by human beings in the planet.

5. Familial longevity refers to families enriched by long living members. On the basis of stringent criteria and accurate analysis of the demographic data in Europe, familial longevity can be identified as that of families where at least two living members aged ≥ 90 years were present.

6. Most genetic studies on human longevity suffer from a variety of limitations due to the difficulty in recruiting large number of phenotypically well characterized long living people (centenarians), small cohort groups, difficulties in validation of the findings in different cohorts in order to test the general meaning of the findings, lack of controls born at the same time as centenarians but with different life span duration and lack of important information such as environmental factors, lifestyle and quality of life, presence and duration of disabilities and diseases.

7. There is evidence identifying some genes related to longevity and ageing. Such genes are included in a variety of signaling pathways, i.e. insulin/insulin-like growth factor (IGF-1), nutrient-sensing (mTOR), oxidative stress and anti-oxidants, control of immune-inflammatory responses and lipid metabolism as well as in mitochondrial DNA (mtDNA). However, more evidence is needed. In addition, it is becoming clear that epigenetic changes linked to diet or to other environmental/life style factors (physical activity, emotional stress) play a role in longevity attainment.

8. Most life-extension effects in animal models have been found to result from knocking down a relatively large number of different genes. This unexpected finding would suggest that the wild-type gene shortens lifespan. It is important to note that the animals with an extended lifespan as a consequence of genetic/environmental manipulations in laboratory conditions show a shorten lifespan when they live in environmental conditions more similar to those of real life. This can be considered "a laboratory trait" in comparison with the centenarians analyzed in studies on human longevity who spent their life in a real and often harsh environment.

9. Combination of animal genetic studies, human genetic population-based and family-based studies, as well as, “omics” studies, are approaches that may help identify genes/pathways (and also biomarkers) involved in ageing/longevity.

10. Caloric restriction, hormonal replacement and antioxidant treatments were reported to promote healthy longevity in some animal models. Also, some strategies for enhancing longevity were introduced e.g. engineered negligible senescence, nucleic acid therapy and cloning of genes related to ageing or genes which could promote longevity. Moreover, mechanisms that affect cell senescence *in vitro* and/or animal ageing may not be fully relevant to humans. Therefore, scientists would always seek definitive clinical evidence and validation of such data in humans.

This is the best way to respond to “commercial” anti-ageing medicine. Other strategies are worthwhile to pursue in humans, such as prevention of vascular events, cancer screening and healthy life style which together have the potential to decrease morbidity and mortality associated with ageing.

These statements are based on the longevity consensus documents [1-9].

CONFLICT OF INTEREST

These recommendations were written independently; no company or institution supported the authors financially or by providing a professional writer. Some of the authors have given talks, attended conferences and participated in trials and advisory boards sponsored by various pharmaceutical companies.

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