Perspectives

Strengthening Systematic Research on Aging: Reflections from an Omics Perspective

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ABSTRACT

Population aging has become a global concern in population development. Challenges to good health in older ages are more complex than at any other age and require a comprehensive framework to move the science of aging and health forward. In this paper, we describe an advanced and evolving conceptual framework that includes definitions, goals, disciplines, and a scope of human aging omics (HAO) based on theories and methods of omics science. The development of HAO will bring a paradigm shift in research related to aging and health by systematic identification, characterization, and quantification of all sets of health conditions and their complex relationships with the internal biomolecules and the external environment in the whole aging process of human beings from birth to death throughout the lifespan.

Population aging has become a key issue to be addressed urgently in global population development. According to World Population Prospects 2022, the share of the global population 65 years and older is expected to increase from 10% in 2022 to 16% in 2050. By then, the number of people 65 years or older will be twice the number of children under 5 years old and roughly equal to the number of children 12 years and under (*1*). China, with the world's largest number of older adults (190 million people aged 65 years or older in 2020) and an extremely fast population aging rate (older people increasing from 8.87% of the population in 2010 to 13.50% in 2020), is facing an even more serious challenge. At the same time, human life expectancy has been increasing. In 2019, the global life expectancy at birth was 72.8 years, an increase of nearly 9 years of life since 1990. Further reduction in mortality is expected to increase the global average life expectancy to 77.2 years in 2050 (*1*). The increase in human life expectancy allows us to pursue a higher goal — an increase in healthy life expectancy, which will not only improve the quality of life but also reduce the overall economic and disease burden, thereby jointly contributing to social development.

In the context of global aging, the promotion of health for older adults is undoubtedly a very urgent and challenging task for a wide range of medical-related policymakers, medical workers, and industry professionals. This is because health for older adults is a complex, three-dimensional, dynamic issue. Externally, it involves policy systems, cultural concepts, economic development, and natural and social environments at the macro level; family and social support at the meso level; and individual behavior, experience, psychology, etc., at the micro level. Internally, it is the cumulative result of the aging of an individual during the lifespan. The aging status at each stage of life is related to health, disease, disability, and death at the next stage. Internal and external interactions form an invisible network of time and space around an individual's health at each age stage, making health at old age present obvious systematic characteristics. For example, in the context of the most pressing current health challenge — the coronavirus disease 2019 (COVID-19) pandemic, older adults show particular vulnerability in terms of susceptibility, death, and secondary diseases after acquiring severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (*2*). This is not a matter of age per se, but of the underlying health disadvantages and vulnerability to risk resistance caused by increasing age.

The challenge of health in older age, which is more complex than health issues at any other stage of life, requires a more comprehensive framework to guide all aspects of the work. The emerging field of population medicine, which integrates basic medicine, clinical medicine, public health and preventive medicine, and rehabilitation medicine, and coordinates individual preventive health care, medical rehabilitation, and the overall health actions of the population to maximize health benefits of the population (*3*), provides a macroscopic choice for this purpose. From a microscopic view, the systematic concept of omics is in line with population medicine.

In the past four decades, "omics" has become a research mechanism and methodology for systematically studying scientific fields such as the life sciences and medicine. In 1920, the botanist Hans Winkler created the term "genome" and then became the first person to use the term "omics" (*4*). In 1986, geneticist Thomas H. Roderick coined the term "genomics" to refer to the study of the structure and function of the entire genome of a living organism by mapping, sequencing, and characterizing genomes (*5*), integrating previous gene-level studies in the life sciences into a systematic scientific system. Subsequently, "transcriptomics", "proteomics", and "metabolomics" came into being, and the use of "omics"-terms continued to expand, forming more macroscopic applications such as "environmental omics" (*6*) and multi-staged data-integrated multi-omics (MS-DIMO) that integrates multiple types of omics data in a single study (*7*). Although, methodologically, the development and application of omics in biomedicine rely on high throughput molecular technologies, in theoretical thinking, the primary goal of various omics is to try to completely describe and understand the structure, function, and dynamics of a given level of research objects (*4*). The maturity and foundation of various types of omics research give important enlightenment to the overall aging and health of human beings; that is, all conditions, including health, disease, and death from the beginning to the end of life, as well as their complex relationships with internal biomolecules and the external environment that form an interlocking systematic "omics" throughout the lifespan, i.e., human aging omics (HAO). This is consistent with the goal of "OMICS 2.0," which promotes omics technologies and their applications in diverse and complementary global settings (*8*).

HAO is an advanced and evolving concept that can be defined as the identification, characterization, and quantification of all sets of the rules of growth, development, maturity, aging, health, disease, injury, disability, rehabilitation, and death and their complex relationships with the internal biomolecules and the external environment in the whole aging process of human beings from birth to death throughout the lifespan. The goals of HAO are to bring people to a better grasp of the laws of life change and aging, to promote a steady increase in health reserves throughout the lifespan, and to improve the ability at an older age to respond to the consequences of health risks accumulated since early life.

The basic discipline of HAO is the combination of biomedicine, which is committed to exploring the laws of aging at the microscopic level, demography that explores the laws of age change from a macroscopic perspective, and medicine and public health, that focus on health outcomes. HAO benefits from the contributions of archaeology, anthropology, psychology, management, and related disciplines. Correspondingly, the research theories and methods involved come from an interdisciplinary system supported by the interaction between the natural and social sciences. HAO can be divided into sub-HAOs according to the characteristics of life periods, such as embryonic development aging omics and puberty aging omics. It can be integrated with other omics to form a more targeted research field, such as embryonic development aging metabolomics. More focused and in-depth research on specific issues can be conducted, such as research on cognitive development aging omics.

The research scope of HAO includes but is not limited to:

Molecular-level measurement of physiological age using omics data. Age is a key risk factor for disease and disability in older adults. To tackle age-related diseases and increase a healthy lifespan requires molecular-level measures of biological age and aging rates that target the aging process to "rejuvenate" physiological functions (*9*). Using high-throughput omics technologies to measure biological aging, exploring the quantitative characterization of aging at molecular resolution, and further determining controllable factors related to physiological aging is the basic work of HAO.

Individual-level research on the health trajectory of aging throughout the lifespan. This is the ultimate exploration of the relationship between aging and health outcomes. The systematic research idea of HAO is the basis for the realization of this research content.

Population-level identification of age-specific risk imprints on lifespan. From the perspective of HAO, the systematic identification of aggregation points of health status and risk categories with age as the context can reveal the aggregation mode, aggregation intensity, risk factors, and their contributions and can change the rules of health reserves of the population. This is conducive to developing of precise health risk control and intervention throughout the lifespan and exploring policy directions for improvement of healthy life expectancy.

Temporal-level evaluation of the health resilience of the population at multiple time points. Exploring the dynamic changes in health reserves and risk defense capabilities from the temporal dimension by taking the whole population of a region or a country as a unit is a macro embodiment of HAO. Researchers can build appropriate indicators to analyze dynamic changes, for example, by using the average annual percent change (AAPC) of the utilization of health services in a population of a certain age and characteristic (*10*) as an indicator to evaluate the health resilience of the population. An increase in AAPC indicates an increase in health resilience.

Policy-level integration of strategies to actively respond to population aging. Health promotion of older adults requires organic cooperation of disease prevention, disease diagnosis, disease and injury treatment, disability rehabilitation, risk control, health education, and other related disciplines. More detailed strategies should especially be taken in areas where socioeconomic development is uneven. This work needs to be systematically integrated from the perspective of HAO to form an organic chain, starting from early life, to improve both high-quality lifespan and health.

With the continuous development of scientific and technological progress, biomedicine, public health, demography, and other disciplines have laid a certain scientific foundation for establishing HAO. Further integrating theories, methods, information, data, and the experiences of omics such as genomics, transcriptomics, proteomics, and metabolomics can expand the scope of omics science to a higher level of research and over a longer time range to carry out aging omics research according to the systematic state of human life. This will undoubtedly contribute to the scientific basis for health management throughout the lifespan and may provide some assistance for human reproduction and survival to better adapt to the environment. At present, the concept of HAO is only in an initial stage, and its definition, content, and research scope need to be continuously enriched and improved. The construction of its preliminary framework (Figure 1) in this paper is precisely to achieve this purpose. Nevertheless, for aging and

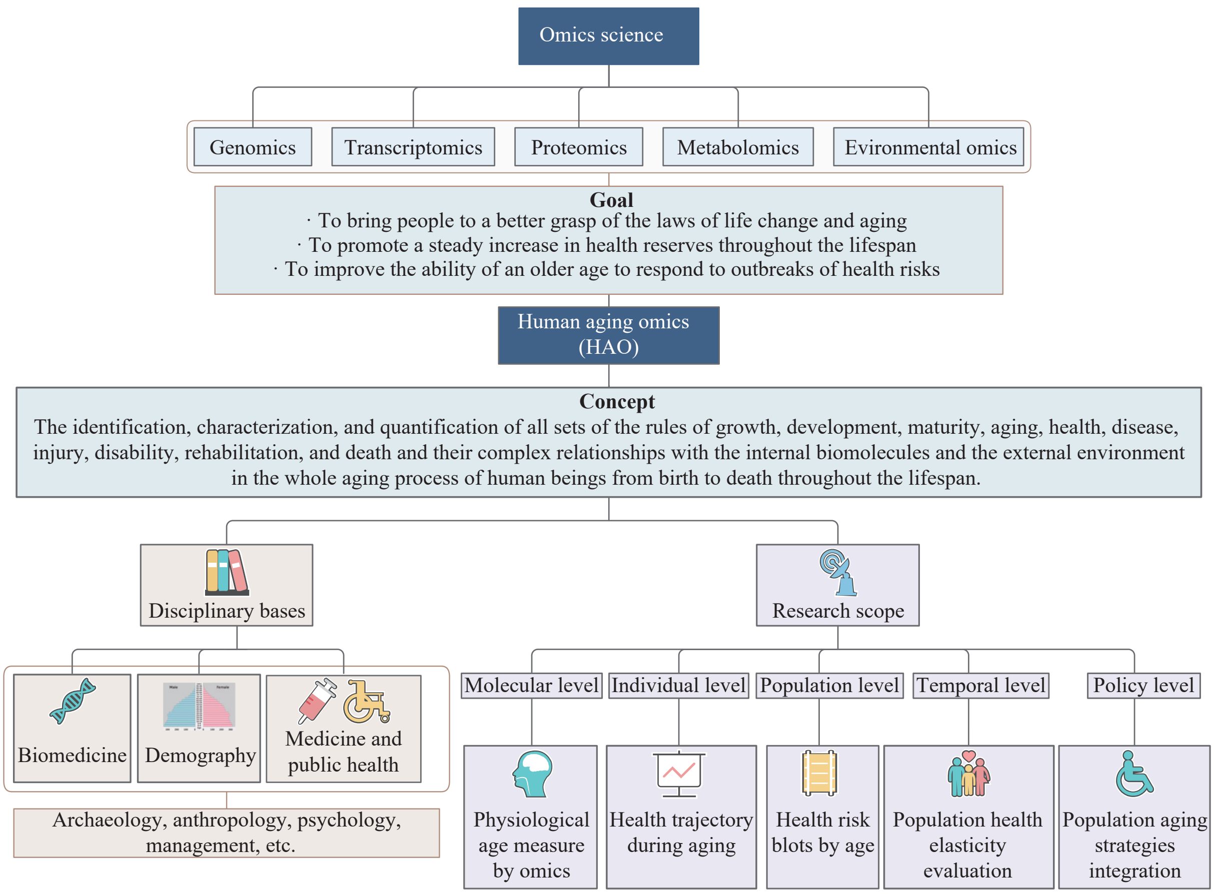

FIGURE 1. A conceptual framework of human aging omics.

health, the most complex, three-dimensional, and dynamic research object, HAO is undoubtedly an innovation in theory and application. The development of HAO will allow the application scope of “omics” not to be confined only to the natural sciences but to encompass systematic, homogeneous unit sets of social sciences and related disciplines and bring about a paradigm shift in research related to aging and health.

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