

## Aging, Health, Hormesis and Future Lines of Investigation

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### Editorial

Biological aging research shows that there are no gerontogenes that have evolved with the specific function of causing aging and determining the time of our death. Genes determine our survival and our ability to live and maintain health, but for about 40-50 years only. This period of life is known as the essential lifespan (ELS), required by evolution for the assurance of life and the continuation of generations. In the presence of survival genes, we are able to live, and now we even expect to live, for much longer duration than our species' ELS. However, a longer life beyond ELS also allows the emergence of aging together with all its physical, mental and social manifestations. That then requires lifestyle adjustments, and biomedical, aesthetic and psycho-social methods for maintaining health and identity in old age.

Aging is thus an emergent phenomenon and happens individually. And so the methods to intervene in aging are also required to be person-specific. The highly complex and dynamic nature of our present bodies makes it impossible to completely stop or reverse aging. The very act of living constantly causes damage in our cells through three major sources of damage: (1) free radicals formed due to external factors (for example, sunlight and pollution), and as a result of internal metabolism involving oxygen and metals; (2) nutritional components, including glucose, fats and their metabolites; and (3) errors in the biochemical processes of DNA duplication, RNA transcription and protein synthesis. Evolution has developed a complex network of molecular, cellular and physiological maintenance and repair systems (MARS) to control the damage and assure the survival during ELS. MARS create a "homeostatic/homeodynamic space", or a "buffering capacity", in terms of stress tolerance, damage control and constant adaptation. There is no state of so-called homeostasis in living systems. Life is dynamic, interactive, adaptive and constantly remodelling.

Life beyond ELS is accompanied by a progressive shrinkage of the homeodynamic space, reduced stress tolerance and increased vulnerability. All negative signs of old age, including age-related diseases, are due to declining efficiency of MARS. Although a variety of cosmetic, nutritional and other lifestyle interventions are being promoted and sold as "anti-aging", a promising scientific approach towards healthy aging is that of hormesis for maintaining health and homeodynamics. Hormesis is the positive relationship between low-level stress and health. Whereas uncontrolled and unwanted stress is negative and harmful, low level "stress of choice" can be good and health beneficial. Moderate exercise is the best example of hormesis. Exercise initially increases the production of free radicals, acids and other harmful biochemicals in the body. But MARS-based cellular responses to this mild stress protect the body and strengthen the homeodynamics. Conditions that induce hormesis are called hormetins, and are categorized as nutritional-, physical- and mental hormetins. Several food components, such as spices, flavonoids, polyphenols and micronutrients are nutritional hormetins. Sauna, breath control, and mental challenge, including meditation, are examples of physical and mental hormetins. Novel combinations of multi-hormetins are under scientific investigation.

Two challenging questions that need to be given high priority in biological aging research are: (1) what is the functional relevance of various types of molecular damage which accumulate during aging? and (2) what are the biological determinants of health and homeodynamic space in terms of stress response profiles, damage control and tolerance, and adaptive abilities? Resolving these issues are crucial with respect to testing, developing and applying effective means of aging interventions for maintaining health and activity in old age.