

Bringing light to applied healthspan engineering, age management medicine and the importance of methylation in health maintenance.

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Abstract

Applied Healthspan Engineering (AHE) is the title of James Larrick and Andrew Mendelsohn's article published in 2010. Based on the fact that all organisms have a minimal level of functional reserve required to sustain life that declines to a point incompatible with survival at the moment of death, AHE seeks to maintain or restore optimal functional reserve of critical tissues and organs. The idea is to avoid the decline that has always been associated with the process of ageing. For that, we need to take action in order to maintain health along our lives.

Keywords: Healthspan, Methylation, Ageing Hypothesis, Nutrigenomics

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Introduction

Invariant rate of ageing hypothesis

It is important to notice that AHE just makes an assumption that stabilizing well-being might result in increased longevity [1], but it must be clear that increased healthspan doesn't necessarily mean increased lifespan, which is a more complex issue. In fact, we have reached an understanding that both knowledge and technology are available and is now actually possible to "square the healthspan curve", as shown in figure 1 [1].

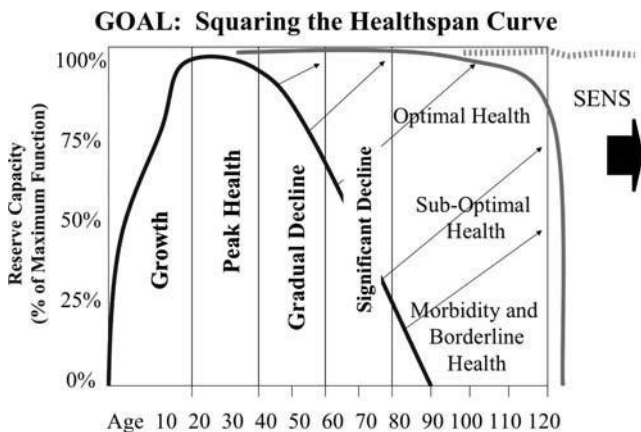


Figure 1. Minimal goal of Applied Healthspan Engineering (AHE) is to square the healthspan curve. Well-being peaks at the end of growth phase (between 20-30 years of age) and then declines. AHE seeks to stabilize well-being.

According to a recent study that tested "the invariant rate of ageing hypothesis" (2021), the rate of ageing seems to be relatively fixed within species and biological constraints affect unstoppably the human rate of ageing [2]. However, along the years there is a process of molecular damage accumulation upon which we can interfere [3].

The damage we refer to are biochemical processes, such as inflammation, oxidation, glycation, acidification and submethylation. By controlling and optimizing these processes, if not delay the process of ageing, we can most certainly delay "the acceleration of the process of ageing" that is usually expected to occur in consequence of inadequate life style choices and stress-related problems, regardless of any existing rate of ageing. This is the approach of the so-called "Age Management Medicine" focused on health maintenance and, consequently, making it unnecessary to act on the prevention of specific diseases, such as cancer, heart disease, Alzheimer and all other diseases related to molecular damage accumulation, including the ageing process itself [4].

Discussion

As far as cancer is concerned, it is well known that inflammation and oxidation are in the basis of tumoral processes [5]. Reinforcing anti-inflammatory and antioxidant protection through the use of an anti-inflammatory diet and supplements may actually protect against cancer [6]. In fact, thousands of articles in the scientific literature have investigated the anti-inflammatory and antioxidant activity of different plants in nature. *Curcuma longa* (turmeric), *Nigella sativa* (black cumin), *Zingiber officinale* (ginger), *Allium sativum* (garlic), *Crocus sativus* (saffron), *Piper nigrum* (black pepper) and *Capsicum annuum* (chili pepper), for example, are spices which contain several anti-inflammatory & antioxidant bioactive compounds, such as curcumin, thymoquinone, piperine and capsaicin [7], and can also be used as supplements. *Pinus pinaster* or French maritime pine bark extract (procyanidin rich) and *Vitis vinifera* L (resveratrol rich) are also anti-inflammatory and antioxidant herbal supplements that have been proposed for preventing and treating a wide range of chronic conditions (5, 8, 9). They are all considered potential sources for the prevention and treatment of cancer [5, 8, 9, 10].

Methylation, on the other hand, particularly DNA methylation - a biological process by which methyl groups are added to the DNA - is another biochemical process which is hardly known by the public, in general, and, even at academic levels, it doesn't seem to receive the attention it deserves. It is the most commonly studied epigenetic process, that is, a mechanism which can influence gene activity without changing the DNA sequence [11].

Most DNA methylation is essential for normal development, and it plays a very important role in a number of key processes including genomic imprinting, X- chromosome inactivation, and suppression of repetitive element transcription and transposition. When dysregulated, DNA methylation contributes to diseases and it is known to be abnormal in all forms of cancer [12]. It is considered a potential biomarker of future health outcomes [13].

But what can we do on a daily basis regarding protection of the DNA from methylation-deficient processes?

The first thing is to deepen our knowledge about Nutrigenomics - a multidisciplinary approach that deals with the effect of foods on our genes and the response of individual genes towards nutrients [14]. It has to be highlighted as of utmost importance in cancer prevention.

Figure 2 shows that mutagens from the diet can make changes in DNA methylation leading to the activation of oncogenes that ultimately cause cancer [14].

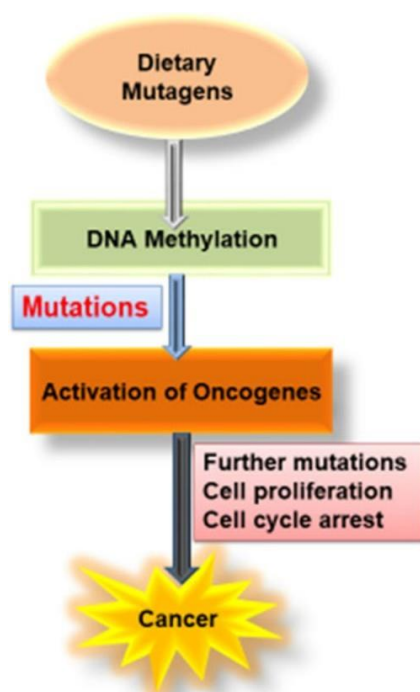


Figure 2. This figure depicts that mutagens from diet make changes in DNA methylation and leads to activation of oncogenes and cancer.

DNA methyltransferase is a nutrient-dependent enzyme involved in methylation, responsible for transferring a methyl

group from S-Adenosyl methionine to particular sites on DNA, being directly responsible for the transformation of chromatin. S-Adenosyl methionine, in turn, takes up its components from food vitamins like B2, B6, B12 and folic acid. Therefore, a very simple cancer prevention approach should include an adequate dietary supply of B complex vitamins. It might also be necessary to use their active forms (such as riboflavin-5-phosphate, pyridoxal-5-phosphate, methylcobalamine and methylfolate) in nutritional supplements. Also, dietary carcinogens, such as aflatoxins, alcohol, heterocyclic amines and nitrosamines, must be avoided [14]. This is certainly a good start to be proactive against cancer.

The aim of this commentary is to bring light at the same time to Larrick & Mendelsohn's article, to the idea of Age Management Medicine and to the role of methylation in this context. It is time that the whole idea of health maintenance becomes better well known, particularly between young medical students. That's because there might be a "gap" between the understanding of how factors (such as poor diet, lack of exercises, stress management problems, sleep deprivation, microbiome imbalances, radiation exposure, toxic contaminations and dietary carcinogens) influence the development of diseases and the manifestation of the diseases themselves. By controlling the molecular damage related to the physiopathological mechanisms involved in the development of diseases, such as inflammation, oxidation and submethylation, we can certainly be avoiding or delaying their manifestation and, most likely, decrease their severity in case they do come to occur.

Last but not least, all these approaches are related to what has been referred to as precision health or precision, personalized medicine. interventions that target to the needs of individual patients on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics [15]. It is a rapidly growing field [16] and has been described as an ongoing revolution in medicine, moving it from a reactive to a "proactive" discipline, where ultimately the objective is "to maximize wellness" for each individual rather than simply to treat diseases [17].

Conclusion

Therefore, the whole idea of health maintenance is very simple and should be made broadly known between medical practitioners and young medical students that might use their creativity to find more and more solutions in order to increase our quality of life along the process of ageing which should be no longer seen as an unavoidable decline.

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Conflict of interest

Authors have no conflict of interest.

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