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Mohammad Rafi  
*Thomas Jefferson University*

Abass Alavi  
*University of Pennsylvania*

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Debate on human aging and lifespan

Mohammad A. Rafi*, Abass Alavi†

*Department of Neurology, Jefferson Medical College, Philadelphia, Pennsylvania, USA
†Department of Radiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA

Summary

The issue of human lifespan has long been a matter of controversy among scientists. In spite of the recent claim by Dong et al that human lifespan is limited to 115 years, with the mounting improvements in biotechnology and scientific understanding of aging, we may be confident that aging will slow down over the course of the current century extending human longevity much longer than 115 years.

In a paper entitled “Evidence for a limit to human lifespan” by Dong et al that was published in Nature Vol. 538 (October 13, 2016), the authors concluded that human lifespan is limited to 115 years and the probability of a lifetime exceeding 125 in any given year is less than 1 in 10000. After about 8 months, the topic is now up for debate again. Five brief communications from different research groups have appeared in Nature Vol. 546 (June 29, 2017), all disagreeing with the paper’s conclusion that the human lifespan is limited to 115 years. The critics have analyzed the paper from different viewpoints. The arguments focus primarily on different aspects of the statistical analysis, the limited availability of data, the splitting of the study period into two ranges (1968–1994 and 1995–2006), the failure to collect and verify the lifespan of extremely long-lived individuals, and the disregard for possible other trajectories. However, the authors of the paper have rejected all of these critics in...
different rebuttal letters (*Nature* Vol. 546) and defended their conclusion of a human lifespan limited to 115 years.

The issue of human lifespan has long been a matter of controversy among scientists. According to Olshansky and Carnes, there are three opposing viewpoints on human longevity, those of “Futurists,” “Optimists,” and “Realists.”

Futurists believe in the continuous extension of human life with no limitation. They rely on forthcoming improvements in different biotechnological domains that will dramatically transform the landscape of human aging and longevity toward a physical immortality and eternal youth.

Optimists believe that the existing increase in life expectancy, which began during the last century, will continue its linear increase at about 2.5 years per decade. Optimists, too, rely on biomedical technologies not currently available and do not foresee any limit to a continuous increase in life expectancy.

Realists, however, argue that human lifespan is biologically determined and that continuous increase in life expectancy is, practically, implausible. They believe that there are many factors interfering with the duration of human life, as well as with the lifespans of other organisms. Aging, itself, is a fact that, according to existing scientific knowledge, cannot be stopped or reversed. It may be slowed down, but it is unlikely to have a perceptible impact on life expectancy. Therefore, Realists believe in the existence of a life boundary that is like a warranty period or expiration date, limiting lifespan and, hence, longevity.

There is no doubt that, due to scientific advances in biotechnology and medicine, human life expectancy has increased during the last century. According to the National Institute on Aging, while the average life expectancy for babies born in 1900 was only 47 years, it rose to 79 years in 1998. Meanwhile, the title for the longest life recorded in human history belongs to the French woman Jeanne Calment, who lived 122 years (1875-1997). It is also notable that the upward course in life expectancy has slowed down during the current century. While the precise limit to human longevity is arguable, based on the current state of our medical and biomedical knowledge, some limit or range of limit is necessary. Therefore, human immortality and eternal life, as supported by Futurists, appears to be out of the question. Clearly, the study done by Dong et al. suffers from restricted sample availability. A more realistic evaluation of human longevity requires not only a longer study duration, which would, in turn, provide an increased sample size but also a carefully designed study plan and data analyzing strategy.

The increase in life expectancy during the last century was mostly due to improvements in public health and achievements in declining early age mortalities. In the future, the escalation in human lifespan will depend on healthier lifestyles and the availability of improved biomedical advances and biotechnologies. With scientific interventions and environmental improvements, we may be confident that aging will slow down over the course of the current century.

Aging may be inevitable, but the rate of aging may not be so if we recognize the causes of aging. What appears to play a more influential role in limiting lifespan is the progressive accumulation of molecular damage inside the cells. While any kind of structural and molecular damage may profoundly affect cell function and accelerate the aging process, damage to DNA structure, because of its vital role in life, has been a focal point, giving rise to the “DNA damage theory of aging.” Both mitochondrial and nuclear DNA damage lead to the development of pathological conditions that accelerate aging and senescence. Fortunately, our cells are equipped with mechanisms that can efficiently repair these damages. However, over time, some of these repair mechanisms may fail or their function may be blocked by other molecules. Therefore, damaged DNA will remain unrepaired and, as time goes on, accumulate, disturbing cell function and affecting lifespan.

One of the DNA repair pathways relies on the restoration activity of “poly-adenosine diphosphate-ribose-polymerase I” (PARP1). The repair function of this enzyme can be inhibited by another protein called “deleted in breast cancer 1” (DBC1). The DBC1 gene was originally found to be deleted in some breast cancer cells. This protein seems to be involved in the regulation of cancer cell energy metabolism. A recent study by Li et al. has revealed that both PARP1 and the oxidized form of “nicotinamide adenine dinucleotide” (NAD+) compete with each other in binding to the DBC1 protein, therefore, keeping PARP1 unblocked and capable of DNA repair.

Experiments conducted in old mice, have shown that age-related DNA damage diminishes when the cellular level of NAD+ is increased. The outcome of these experiments suggests that as NAD+ levels decline with age, fewer NAD+ molecules are available to prevent DBC1 binding PARP1. Therefore, unblocked DBC1 will bind PARP1 and damaged DNA will remain unrepaired. The accumulation of the unrepaired DNA, over time, will gradually paralyze cell function. In an increased abundance of NAD+, the harmful action of DBC1 will be stopped and DNA repair with PARP1 will continue slowing down the aging process.

Another study just published in Nature (July 26, 2017) demonstrates the role of renewed neuro-stem cells (NSCs) in the hypothalamic region of the mouse brain. While the pivotal role of the hypothalamus in whole body aging was shown previously, in this study the authors demonstrated that besides the known neurogenesis role of the hypothalamic NSCs, these cells contribute greatly in the production of exosomal microRNAs (miRNAs) in the cerebrospinal fluid. These exosomes, which are linked to the neuro-stem cell function, and therefore, to whole body aging, can be produced from the cultured hypothalamic NSCs and delivered to the brain hypothalamic area. While the exosomal miRNAs production declines during aging, their increased level in the treated mice leads to slow down the aging process.
Given the crucial biological differences between mice and humans, the applicability of these treatments in humans and their positive results remain to be seen. In the best case of scenario, expecting an increase in average life expectancy for young generations of about 100 years and longevity over 125 years appears to be reasonable.

Competing interests
The author declares no competing interests.

Ethical approval
There is none to be declared.

References