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Berkeley Scientific Journal

Title

Aging and Immortality

Permalink

<https://escholarship.org/uc/item/64k6x6s4>

Journal

Berkeley Scientific Journal, 21(1)

ISSN

1097-0967

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Publication Date

2016

DOI

10.5070/BS3211033755

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Undergraduate



AGING AND IMMORTALITY

BY DANIEL JIAO

The oldest verified person lived to 122 years old and died in 1997 but even today we have people claiming to be even older such as Mbah Gotho who states he is 145 years old. The current worldwide average expectancy is 71 years old but the variety of ages we live to is enormous. We still have much to learn about what leads to these differences in life spans leading us to question what aging is. Numerous studies have been done investigating the various causes of aging such as telomerase, mitochondrial signaling, sensory signaling, diet, and microRNAs. Telomerase is an RNA dependent DNA polymerase which is used to lengthen the ends of chromosomes by adding base pairs. The ends of each of the arms of the chromosome are called telomeres and they protect the cell from losing important coding regions on chromosomes. Base pairs are lost from the chromosome ends upon each division which slowly shorten the telomere. This continues until a point at which the cell can no longer divide which is called cellular senescence. The cell is then able to kill itself by the apoptotic pathway when the critical length is met during cellular senescence. In the end all telomeres are controlled by the telomerase activity and erosion during cell division and it is one of the reason why organisms such as humans cannot live forever currently. The idea that the shortening of telomeres and apoptosis is important in regulation of tumor suppression is strongly supported

Investigations into the telomeres of different organisms such as lobsters can provide greater insight into their role and functions in aging. Lobster are known to have indeterminate growth meaning that they continue to grow until they die. This is unlike humans which have determinate growth and stop growing mostly after puberty. We can then think about chromosomal shortening and why lobsters are able to replicate their cells continuously but humans are not. The answer is the lobster's telomerase which is continuously produced even after maturation of the tissues which is unlike human cells which mostly exhibit no telomerase activity after differentiation. Telomerase is only one of the many factors that plays a role in aging however so even though lobsters theoretically can keep dividing their cells continuously they usually live 30-50 years depending on gender. The fact that lobsters do not live forever or for unreasonable years shows that other factors play huge roles in determining life span such as mutations, diseases, and diet.

Studies done on telomerase and genetics are often extremely difficult to do on humans but luckily even animal models can provide tremendous information about humans. We can then look at less complicated organisms such as *Daphnia pulex* (clone RW20) and *Daphnia pulex* (clone Lake XVI-11) also known as a water fleas. TRAP assays were used to compare the telomerase activity in both these species and measure the telomerase activity at certain points in their life in an equal and controlled environment. The results showed that *D. pulex* showed a steady decrease in telomerase activity as it aged while *D. pulex* kept its telomerase activity with a significant increase in telomerase activity from 1 week to 2 weeks old and less significant increases after that. *D. pulex* (RW20) only had a median lifespan on 16 days compared to *D. pulex* which had an average lifespan of 79 days. The further testing showed that at around week 1 both species had similar telomerase lengths but after the first week *D. pulex* exhibited significant telomere shortening while *D. pulex* exhibited no shortening. This is the opposite of what one expects because *D. pulex* lives around 5 times longer than *D. pulex* however it exhibits telomere shortening while *D. pulex* does not. This study is a significant verification that telomerase is only a small part of the process of aging and determining life span.

One last thing to look at is not an organism itself but a cellular anomaly in humans, cancer. Cancer cells in particular need telomerase activity because of their continuous division and growth which eventually leads to a person death. With telomere shortening in normal cells we are able to prevent tumors by limiting the number of times a cell can divide in mutations towards tumors occurs. It is well known that one of the greatest indicators of serious malignant tumors is the reactivation of telomerase. The studies have also indicated that cancer cells have usually the same length telomeres or shorter than the surrounding tissues indicating a lack of overexpression of telomerase. There are occasions where cancers use overactive telomerases and produce longer telomeres but that applies to less than 10% of cancers

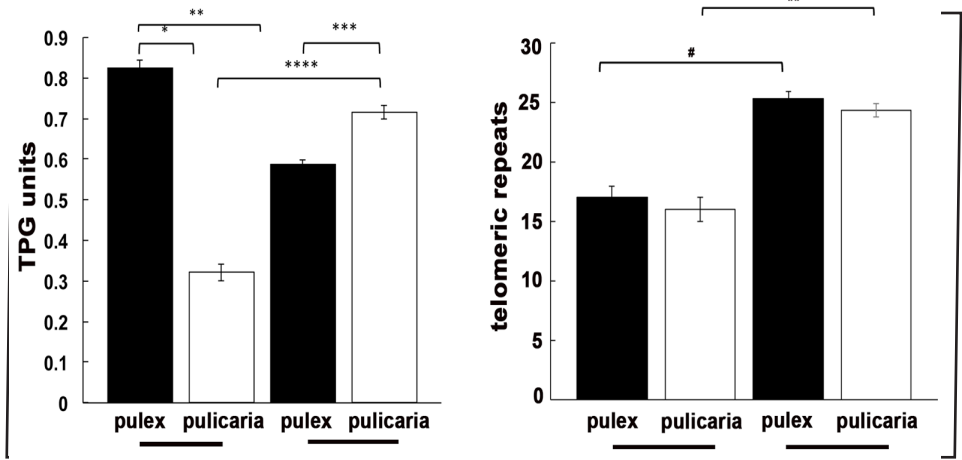


Figure 1: Daphnia life spans

compared to normal telomeres or shorter telomeres observed in around 90% of the cases of cancer cells. Telomerase is a huge factor in cancer cells life cycle and is now a target for anti-cancer therapeutic drugs since most human somatic cells do not produce telomerase.

We can see that telomerase plays a significant part in aging in many ways but in some instances less than one may expect. Telomerase investigation and further research can allow us to provide many different breakthroughs from extended life spans to cancer treatments. There are many other factors we must consider when we look at aging and perhaps telomerase is not the current limiting factor however it can be applied to many function understandings of other diseases as lack of telomerase activity can be seen in many genetically inherited and early onset diseases. While we look at the activity of telomerase within organisms we see not as much influence as one may expect. It is possible that the telomeres are already designed quite efficiently and long enough that telomeres are rarely often the causes of diseases and death but this is another area of research that needs to be looked into. The overall impact telomerase research is limitless at this point with its vast applications.

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