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# Hayflick Limit: A Constraint in Eternal Life

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**SUMMARY**

This article unravels the covert genetic mechanisms of cellular aging. Through Hayflick limit hidden potentials of mankind development in future can be uncovered. There could also be a probability that key to unlock the obscurities in increasing the human life expectancy underlies in one of the most lethal factors, cancer, but the current technologies are incompetent to explore this possibility. Further research in this field can open the locks lying on the improvement of human life.

## INTRODUCTION

Every organism aims to pass on its legacy to its next generation. This falls true even at the fundamental level of cells. Cells aim to achieve this through cell division. But it is beknown that death of every living organism is decided ever since its birth. This also holds true for cells and hence the cellular aging begins with cell division. Simply stated, this means that process involved in giving life to new cells is also involved in death of older cells.

### History

The older concepts based on the experiments of Alexis Carrel suggested that all the cells are immortal in nature. But modern experimental approaches by Leonard Hayflick upturned a 60 year old dogma that all the cultured cells are immortal and proved that only cancer cells are immortal and normal cells are mortal i.e. a signal of aging at the cellular level.

### Hayflick limit

A closer look on genetic mechanisms involved in cellular aging and mortality of cells explicates some of very interesting phenomenon to be taking place at molecular levels. Aging of cells begin as early as the first cell divides. This means that normal cells have a mechanism for reminiscing what replication level they are at. This mechanism is called as Hayflick limit, or Hayflick phenomenon. The Hayflick limit is the number of times a normal somatic, differentiated human cell population will divide before cell division stops. Thus, it is the uppermost limit of cell division after which cell enters senescence. A normal human fetal cell population will divide between 40 and 60 (50±10) times in cell culture before entering a senescence phase which means that normal human cells have restricted capacity for replication i.e. they can divide for a restricted number of times.

### Mechanism behind Hayflick limit and cellular aging

The concept of Hayflick limit starts working from the beginning of cell division process. In cell division, during S phase, the DNA in chromosomes replicates and the amount of DNA per chromosome and per cell is increased twofold. But in telomere, a highly repetitive GC rich heterochromatic region near the end of chromosome, slight deviation in the process is observed. DNA in the telomeric region is not replicated but is synthesised by the process of reverse transcription via enzyme telomerase/reverse transcriptase. This enzyme consists of protein and RNA primers. These RNA primers are continuously used as template to synthesise DNA, i. e., reverse transcription, resulting in repetitive units in telomeric DNA. Now in succeeding generations of cell division, the length of telomeric DNA gets curtailed by one repeating unit. Once the telomere length reaches a critical limit, no further cell division can take place and cell enters apoptosis. Thus, each time a cell undergoes mitosis, the telomeres on the ends of each chromosome shorten slightly. Cell division will terminate once telomeres shorten to a critical length. Hayflick inferred his discovery to be aging at the cellular level. Each cell evolving from cell division is assigned with the Hayflick limit of its antecedent minus 1. If a cell shows Hayflick limit of 1 or less during testing, it is marked with light blue and will die at a Hayflick limit of 0 or less. So, to recapitulate the above information it can be simplified as when the cell division begins, the DNA in chromosomes replicate completely apart from the telomeric region. Telomeric DNA is not replicated but gets synthesised and in the process, a part of telomere gets curtailed with each generation of cell division i.e. cellular aging begins which ultimately leads to apoptosis of the cell and the cell dies.

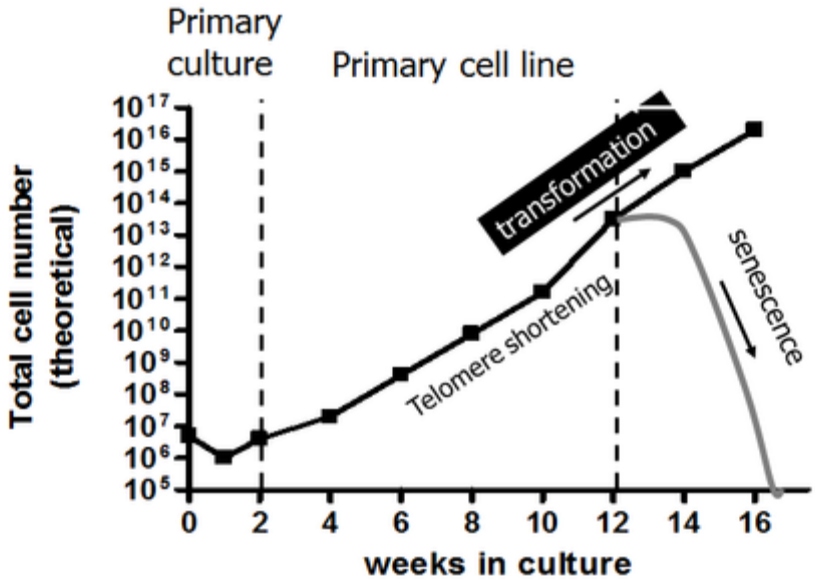


**Fig: Shortening of telomere leads to senescence of cells.**

**Cancer in relation to cellular aging**

An anomaly to the whole process is oncogenic cells. In oncogenic cells, human telomerase gene hTERT promoter mutation and mutations in genes that are engaged in the alternative lengthening of telomere pathways such as ATRX, DAXX offer maintenance pathways that are used to stretch the telomere length in cells. This gives rise to tumours and may ultimately result in cancer cells. Cancer cells achieve a proliferative immortality by multiplying the silent HERT gene that codes for reverse transcriptase enzyme to elongate the telomere in order to circumvent senescence. In simple words, cancer cells contain large amount of telomerase enzyme to elongate their telomere which prevents their aging and turning them into immortal cells.

**CONCLUSION**

Thus, in conclusion it can be said that Hayflick limit effectually establishes the association among various topics of genetics. Hayflick limit unambiguously states that cell division, DNA replication, telomere synthesis, reverse transcription are not separate subjects but are interrelated and different sides of same subject. They together contribute towards the aging at fundamental level. Further research and future prospectives in this field could also lead to advances like anti-aging medicines and technologies that could increase the human life expectancy.

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