Telomerase, Cancer, and Aging

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Abstract

Telomerase is a ribonucleoprotein that works to protect the ends of the chromosome from fraying after rounds of replication by maintaining the telomere length. Its relationship with cancer and aging has been cited by many research studies in the past, as it may be the causal agent of death, but it may also hold a key to immortality. In the absence of telomerase, a cell can divide a certain number of times until telomeres at the ends of the DNA are degraded from many cycles of replication. The purpose of this project is to determine the correlation between the Hayflick limit and telomerase activity by using an exponential regression model. Suggestions are made on how to influence telomerase to increase longevity and decrease cancer.

Problem Statement

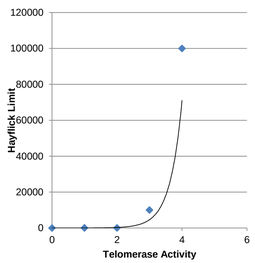
The **Hayflick limit** is a theoretical maximum value of replications a single cell can undergo before it is no longer able to divide and enters either the senescence phase or apoptosis.

Telomeres are the structures composed of a unique DNA nucleotide sequence repeats of TTAGGG complementary double strands and specific coat proteins. During replication 100-200 nucleotide base pairs of DNA are lost after every round of DNA replication. In the presence of telomeres, the telomeric DNA are lost after each DNA replication to prevent the nucleotides that encode genes from being lost.

We observe the Hayflick limit and its relation to telomerase activity in seven different types of cells, which are bacteria *Escherichia coli* (*E. coli*), human fibroblast cells *in vitro*, human stem cell in bone marrow, human tumor cells *in vitro*, human neurons, human mucosal epithelial cells from small intestines, and human follicular cells in ovaries.

Mathematical Approach

The Hayflick limit of follicular cells in ovaries was computed by the conversion of the approximated number of follicles at birth, 295,000 to the algebraic form 2^n (9). The variable n denotes the Hayflick limit value. The Hayflick limit of mucosal epithelial cells was computed in the same manner, using $5X10^{14} = 2^n$ (6).



$y = 1.2852e^{2.7298x}$

Types of Cells	X (Telomerase Activity)	Y (Hayflick Limit)	Log Y
E. coli	0	50000	
Fibroblasts in vitro	1	55	1.740362689
Stem cells (bone marrow)	3	10000	4
Tumor cells invitro	4	100000	5
Neurons in body	0	1	0
Mucosal epithelial cells	1	50	1.698970004
Follicular cells in ovaries	2	18	1.255272505

The Hayflick values were used as dependent Y variables, and telomerase activity was converted into a degree ranging from 0 to 4 and were used as independent X variables.

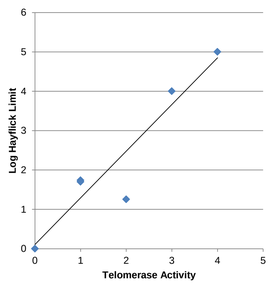
The exponential regression equation $q = Ar^t$ ($q = 1.2852e^{2.7298x}$) was then used to compute linear regression equation in the form of $y = mx + b$.

m = slope of the linear regression line

b = y-intercept of the linear regression line

This yielded the final equation of $y = 1.1855x + 0.109$.

$$q = Ar^t$$
$$log(q) = log(Ar^t)$$
$$log(q) = log(A) + t\,log(r)$$
$$y = b + mx$$



$y = 1.1855x + 0.109$

Discussion

The linear regression analysis yielded an equation of $y = 1.1855x + 0.109$ and R^2 value of 0.88347. The R^2 value indicates that the correlation between the telomerase activity and the number of times a cell divides is significant.

Data suggests that cells with greater regenerative properties possess higher telomerase activity. These include germ cells, stem cells, and cancer cells.

•The Hayflick limit of ***E. coli*** was used as visual comparison to the values of human cells. With an exception of *E. coli* N15 prophage plasmid, *E. coli* cells do not have have linear plasmids and telomeres (2).

•**Bone marrow stem cells** divide indefinitely. Unlike cancer cells, however, bone marrow stem cells are subjected to aging and senescence (8).

•Immortal cells such as **cancer tumor cells** do not lose telomere length with cell division and are strongly identified with telomerase activity. Immortal cells express at least 1000 times more telomerase activity than normal somatic cells (7).

•**Human fibroblasts** divide approximately 55 times before reaching senescence. Fibroblasts do not express hTERT and thus have no telomerase activity in vivo (3, 4). However, the telomerase activity may be induced in vitro by expression of the c-Myc gene, which stabilizes the telomeres (10).

•**Mucosal epithelial cells** in small intestines possess telomerase activity in intestinal crypts (8, 10). In vitro, telomerase may be induced by c-Myc gene and HPV-16 E6 protein activation (10).

Telomerase activity in **follicular cells in ovaries** varies by the stage of oocytes, as it is active in early antral follicles, preovulatory follicles, and ovulated oocytes, but the level of telomerase decreases during oocyte maturation (1, 5).

Conclusions

Based on the regression analysis computed in this project, we conclude that there is a high correlation in the theoretical maximum number of cell divisions and telomerase activity in human cells. A direction for research that could provide beneficial knowledge of aging and cancer would be the finding of a regulatory mechanism of telomerase that would maintain the length of the telomere. The goal of research on telomerase and cancer should be focused on transforming cancer cells to enter the senescence phase or apoptosis. Other factors in aging, such as environmental stress and diseases must be taken into account as well.

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