Synopsis of Original Research Paper

Molecular cloning of novel genes involved in the aging

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In the somatic cells of humans, the telomere repeats have been proposed to provide each cell with a counting mechanism that helps prevent the unlimited proliferation of wayward cells in adult tissues. According to this idea, somatic cells are born with a full complement of telomeric repeats; howevwr, the telomerase enzyme, hTERT, is turned off in a tissue like the skin, so that each time a cell divides, it loses 50-100 nucleotides from each of its telomeres. After many cell generations, the descendent cells will inherit defective chromosomes and consequently will withdraw permanently from the cell cycle and cease dividing-a process called replicative cell senescence. In theory, such a mechanism could provide a safeguard against the uncontrolled cell proliferation of abnormal cells in somatic tissues.

The idea that telomere length acts as a “measuring stick” to count cell division and thereby regulate the cell’s life time has been tested in several ways. For certain types of human cells grown in tissue culture, the experimental results support the theory. However, the molecular mechanism of replicative cell senescence remains unknown. To investigate this process, we tried to identify new genes, those are involved in the process of replicative cell senescence by the method using ribozyme library. In addition, we examined the transcriptional regulation of hTERT, a human telomerase enzyme. hTERT expression is regulated by the methylation status of its promoter region. To express the TERT, the promoter region should be hypermethylated. In contrast, in somatic cells, the promoter region of TERT is hypomethylated to inhibit the expression of TERT gene. Therefore, we tried to examine the regulation mechanism for DNA methylation and demethylation.