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Guest Editorial

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The Nobel Prize in Physiology or Medicine 2009 has been awarded ‘for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase’ to Elizabeth H. Blackburn, from the University of California – San Francisco (USA), Carol W. Greider from the Johns Hopkins University School of Medicine – Baltimore (USA) and Jack W. Szostak, the Harvard Medical School – Boston (USA).

The original trekking started with a basic question in cell molecular biology: how do cells divide? This is the question that both in its form and its implications has been on the minds of biologists, physiologists and even ordinary men for quite some time. For the scientists, it poses a long-lasting query to understand the process of cell division. For the common man, it has been associated with a hope for extending the youth zone and delaying the aging process.

Generally speaking the most important part in cell division is the making of an exact copy (duplication) of genetic material (chromosomes). The importance of this statement is verified when we look back at the number of Nobel prizes that have been given for work on this process of duplication of chromosomes in cells. It started with Hermann Muller who won Nobel Prize in 1946 and then Barbara McClintock who won Nobel Prize in 1983; they found that broken chromosomes were unstable because truncated chromosomes tend to attach to one another, while the chromosome ends were generally stable during cell division. Due to this special nature, they were named *telomeres* (from the Greek words *telos* meaning ‘end’ and *meros* meaning ‘part’) by Muller. However, the structure of telomeres was not known.

In 1975, Elizabeth Blackburn arrived in the laboratory of Joseph Gall at Yale. A single cell organism – *Tetrahymen thermophila* – was used in her studies and by cutting its chromosome into smaller pieces, she found out that the end-sequence of its chromosome was repeat of the six nucleotides CCCCAA. By the same time Jack Szostak had established his own laboratory at the Harvard Medical School where he studied ‘minichromosomes’ – the artificially synthesized genetic material of yeast and found that they were also very unstable and tended to attach to one another. Elizabeth Blackburn and Jack Szostak attended the Gordon Conference in 1980 where they decided to work together to see whether putting the repeats of end-sequence from *Tetrahymena* to the ‘minichromosomes’ could make them more stable. To their surprise they found that it worked!

Now the question was how these end-sequences (*telomeres*) were synthesized *in situ*. The role of an enzyme was speculated. Carol Greider had joined to the Blackburn's laboratory as a graduate student at Berkeley. She discovered the presence of enzymatic activity in the yeast cells when an artificially made primer (opposite sequence to the six nucleotides of telomeres) was added. Greider and Blackburn showed that the enzyme, named *telomerase*, was comprised of two parts – protein and RNA. Thus, telomerase was found to be an enzyme with a protein part which was enzymatic and an RNA part which was the base for the enzyme to act. At last, both *telomeres* and *telomerase* were discovered and characterized.

This discovery has paved the way to explore the process of cell division in a little more detailed manner. Most of the details of division were known except how the tail portions of chromosomes are duplicated as the enzyme responsible for chromosomal duplication (*DNA polymerase* that brought Nobel Prize to Arthur Kornberg in 1959) was found to be unable to copy these end-portions. With the discovery of telomeres and telomerase, the underlying process has become further clearer.

The process of aging has been associated with decrease in the dividing capacity of cells with an exact copy of chromosomes. It is known that shortening of telomeres – that occurs normally with time – leads to the abnormal attaching of chromosomes to each other, and that not being able to separate after cell division, it leads to the presence of defective chromosomes in the divided cells. These defective chromosomes lead to increased chances of defect in the genotypes and thus decrease in the normal functions carried about by these genes leading to progressive loss of division capacity of the cell and hence resulting in aging.

The secret behind eternal youth has been explored both scientifically and metaphysically but the quest for a *fountain of youth* as told in the mythology or an *elixir of youth* as believed by alchemists always ended with disappointments. The present discovery has given us hope afresh for we now understand cell division in a little more details, and thus maybe someday we can effectively stop – and even reverse – the harmful changes in the chromosomes that occur with each successive cell division, and thereby delay the process of aging and prolong the youth zone. Also, in cancer cells there is an increase in telomerase activity. So therapeutic strategies are being designed to block the activity of telomerase in cancer cells, and trials are going on with the hope that by decreasing telomerase activity in cancer cells, we shall be able to combat cancer in future.

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