Aging process – A telomeric insight and need for plants perspective

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Telomere research is an exciting area in biomedical science and three scientists who received the Nobel Prize last year are pioneers in the field. Researchers said that it will be possible to tell whether a person's "biological age", as measured by the length of their telomeres, is older or younger than their actual chronological age. Scientists believe that telomeres are one of the most important and accurate indicators of the speed at which a person is ageing. The size of the telomere of chromosome can determine the age of the person; it means chromosomes with shorter telomere, the small life span of that particular person1.

The structure of telomeres in a wide variety of organisms has been studied to demonstrate that telomeres are highly conserved elements in animals as well as in plants, both in structure and function2. Telomeric DNA has been shown to consist of simple randomly repeated sequences, characterized by clusters of G residues in one strand and C residues in the other. Another feature is a 3' overhang (12-16 nucleotides in length) of the G-rich strand. The repeated telomeric DNA sequence found in *Homo sapiens* is AGGTT and in *Arabidopsis* is AGGGTTT. The same repeated sequence is found at the end of all chromosomes in a species and the same sequence may occur in widely divergent species, such as *Saccharmyces cerevisiae* [(A)$G_{(2-5)}$TTAC] to *Homo sapiens* (AGGTT). At every telomere, as much as 10 kelobases of this repeat sequence may occur. The telomeric DNA is also complexed with non-histone proteins and it is synthesized under the influence of telomerase enzyme (which has reverse transcriptase activity).

The length of telomere is monitored in chromosomes, because uncontrolled activity of telomerase will lead to indefinite elongation of telomeres. Proteins binding to telomere repeats have been identified, which block the elongation of telomeres. These include Rap1p in budding yeast, Taz1p in fission yeast and TRF in humans. Ku and Sir proteins also associated with telomeres, which are shown to be involved in telomere replication and telomere silencing. Again, they may also play some role in regulating the length of telomere3. Each time a cell divides, the process does not copy all the DNA information (the telomeres are not copied). When the cell is finished dividing, the DNA comes back together. The telomeres lose a little bit of length, each time this happens. The telomeres get shorter each time a cell divides, (like a pencil eraser gets shorter each time it's used). When the telomere becomes too short, essential parts of the DNA can be damaged in the replication process. Scientists have noticed that cells stop replication when telomeres are shorter. In humans, a cell replicates about 50 times before the telomeres become too short (Hayflick limit).

We can use the length of a cell's telomeres to determine the cell's age and how many more times it will replicate. This is important in anti-aging research. When a cell stops replicating, it enters into a period of decline (cell senescence), which is the cellular equivalent of aging. It is known that people who are born with shorter telomeres than normal have a shorter lifespan. But still it is not clear whether longer telomeres are responsible for longer lifespan. Geneticist Richard Cawthon at the University of Utah found that shorter telomeres are associated with shorter lives. Among people older than 60, those with shorter telomeres were three times more likely to die from heart disease and eight times more likely to die from infectious disease.

Every system in our body is carefully balanced to allow for cells replicating and dying. If cells stop dying and keep replicating, the balance is disrupted and there are too many of one kind of cell. It is believed that cancer cells are creating an enzyme (telomerase), which prevents telomere shortening. Every cell in our body has the genetic code to make telomerase, but only certain cells need to produce this enzyme[4]. For example, white blood cells and sperm cells need to have telomere shortening switched off in order to make more than 50 copies of themselves through our lifetime. If telomerase could be used routinely to "immortalize" human cells, it would be theoretically possible to mass produce any human cell for transplantation, including insulin-producing cells to cure diabetic patients, muscle cells for muscular dystrophy, cartilage cells for people with certain kinds of arthritis, and skin cells for people with severe burns and wounds. Efforts to test new drugs and gene therapies also would be helped by an unlimited supply of normal human cells grown in the laboratory.

Now, a simple blood test tells us how long we will live. The test will be able to offer the possibility of estimating how long the person has left to live by measuring telomeres on the tip of their chromosomes, the most

important and accurate indicators of how rapidly someone is ageing. However, the test could provide insights into a range of age-related disorders (*i.e.* cardiovascular diseases, cancer etc.).

Maria Blasco of the Spanish National Cancer Research Centre in Madrid is the inventor of this new commercial telomere test. The special thing about this test is that it is very precise. It can detect very small differences in telomere length and it is very simple and fast technique where many samples can be analyzed at the same time. Most importantly, it is possible to determine the presence of dangerous telomeres (those that are very short) by this test.

The 435 Euro ($700) test, will be available in Europe at the end of the year, measures the length of telomeres on a person's chromosomes, which are thought to be linked to longevity. The test looks for high concentrations of short telomeres, which correlate with an increase in biological age. However, the scientists do not yet believe they can narrow down the test prediction to calculate the exact number of months and years a person has yet to live, but studies have indicated that individuals with telomeres that shorter than normal are likely to die younger than those with longer ones[1].

The above research deals with animals only, then what about plants? A plant with shorter telomere will also have shorter lifespan? If it is so, than what will be the age of plants raised through cell or tissue cultures techniques and the transgenic plants. Plant cells can be grown indefinitely for the production of phytochemicals or secondary metabolites in bioreactors. Is the life of plant cells can be also determined with help of such types of tests? So that cells with longer telomere can be used for the commercial production of phytochemicals and the commercial use of micropropagation technology for better and long lifespan clones. A study in this regard will be interesting and useful.

Medical researchers believe that telomere testing will become widespread within the next five or 10 years, but there are already some scientists who question its value and whether there should be stronger ethical controls over its wider use. In addition to concerns about how people will react to a test for how old they really are, some scientists are worried that telomere testing may be hijacked by unscrupulous organizations trying to peddle unproven anti-ageing remedies and other fake elixirs of life. Another worrying thing is that if this information ever got to a point where it is believable, insurance companies would start requiring it in terms of insuring people. If someone smokes or obese, his/her insurance rates will be higher, and if somebody has short telomeres his/her insurance rates might be higher too.

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