Telomeres: our cells' biological ageing clock

By Eleanor Mason, Science Editor (2016/17)
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IN 1953, JAMES Watson and Francis Crick were co-originators in the discovery of the double helix structure of DNA (deoxyribonucleic acid). This discovery marked a milestone in scientific progress that has given rise to research into the function, structure and control of our genetic material. DNA is the macromolecule that allows our genes to create proteins and control chemical processes within the human body.

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The discovery of the 'ACTG' DNA bases, and since then the discovery of introns and exons, promotor regions, insertion elements, 5' and 3' ends, enhancer sequences and the understanding of many other functional and structural components of DNA have contributed to the understanding of our genetic makeup. However, the mechanism in which our long, string-like DNA structures, or chromosomes, encode a biological ageing clock within us was a more recent discovery.

The method by which our chromosomes can be replicated completely during cell division without degradation was a question scientists were pondering for a long time. In 2009, the Nobel Prize in Physiology or Medicine was awarded to Elizabeth H Blackburn, Carol W Greider and Jack W Szostak for the discovery of "how chromosomes are protected by telomeres and enzyme telomerase". Telomeres are repeated nucleotide sequences found at the ends of chromosomal DNA. During cell division, the two complementary strands of DNA separate, with each strand using leading and lagging replication, with the lagging strand elongating continuously u s i n g o n l y o n e primer (a short strand of DNA). However, the lagging strand requires smaller fragments and multiple primers in order to produce a complementary strand due to the direction of replication. It is this lagging strand that falls short each round of cell division. Even if a primer were built at the very end of the chromosome, it would still not be complete.

Therefore, chromosomes would progressively shorten during each replication cycle. However, the three Laureates of the Nobel Prize in 2009 discovered how some of our cells combat this degradation: telomeres and the enzyme that forms them – telomerase. As early as the 1930s, scientists had discovered that the structures at the end of chromosome DNA (telomeres) prevented the chromosomes from attaching to each other, and therefore held a protective role. When the ends of the lagging strand shortens, telomerase recognises the tip of an existing repeat sequence (telomere). Using an RNA template within the enzyme, the template strand is lengthened by adding additional repeats – the telomere returns around its original length. When telomerase lengthens the original template strand, it allows additional lagging strand replication by DNA Polymerase I. So, the actual lengthening of the new strand is not done by telomerase. Telomerase just provides more template.

It was discovered that if these telomeres are shortened, cells age. Conversely, if telomerase activity is

high and telomere length maintained , cell death is delayed. However, this may not prove the answer to a longer life; somatic cells (all cells apart from stem and sex cells) do not express telomerase. In these cells, telomeres do not maintain their length throughout DNA replication, hence why our cells inevitably die, whereas cancer cells are considered to have an eternal life and have high telomerase activity.

Telomeres have two roles: they prevent chromosome shortening by protecting the ends from being used in 'repair' which would lead to chromosome fusions and genome instability, and they act as a damage sensor and trigger senescence if there are any problems. In bacteria, the answer to this problem is simple. Bacterial organisms contain a circular, single structure of DNA . Their replication occurs from a single point, called bidirectional replication. Adenoviruses do not use primers. Instead, they use terminal proteins that bind to the DNA and provides a ligand to prime the synthesis of a new strand of DNA (replication). As higher organisms, such as some human cells, use telomeres, they also require telomerase , which is a reverse transcriptase (an enzyme used to produce a complementary DNA molecule from an RNA molecule).

Without telomerase, the telomeres shrink and once completely gone, the cells die via senescence or proliferation arrest, which explains the inevitable death of our cells. The number of times a human cell, from a newborn baby, can divide on a static medium is around 50, person who is 100 years of age has cells able to divide around 10 times and cells from a newly formed embryo could divide 100+ times. Once this number has been reached, the cell can no longer replicate, thus provoking the onset of age

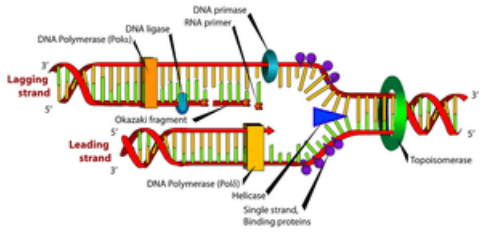

Image: Pixabay

-related factors. The mechanism of controlling telomere length is impressive. Artificial lengthening, or shortening of telomeres in yeast, showed that the organism has homeostasis between telomere lengths as the cells prefer maintain uniform length. The way in which cells measure their telomeres is via a protein called Rap1; when modified, Rap1, which binds to normal DNA, was added and the cells thought the telomeres were longer than they were so they destroyed their ends. This shows that the presence of Rap1 dictates the length of the telomeres. Although the role of telomerase on slowing telomere shrinkage has been discovered, environmental stress and genetic defects can speed it up. However, many studies within this field are not peer reviewed, which makes research in this area questionable.

It seems telomere shortening could be the reason for ageing and decreased healthspan- not just individual cells but the organism as a whole. However, research in this field has shown ageing to be extremely complex and to depend on several factors – telomeres being one of them. Research in this area remains intense.

4 comments

Bill Andrews 9 Mar '17 at 10:38 pm

See https://drive.google.com/drive/folders/0B7kYte_CAcVpQXY3TEdqT0M1S2M
It was stated in the article that: "Telomeres have three roles: they prevent chromosome shortening; they protect the ends from being used in 'repair' which would lead to chromosome fusions and genome instability, and they act as a damage sensor and trigger senescence if there are any problems." But, in fact, they play only two roles because "they prevent chromosome shortening [by] protecting the ends

from being used in 'repair'"
A human cell can divide 50 times if obtained from a newborn baby. A cell obtained from a newly formed embryo can divide 100+ times. And, a cell obtained from someone 100 years old can divide less than 10 times.
In short telomerase doesn't just increase lifespan, it increases healthspan.

Report

Bill Andrews 9 Mar '17 at 10:42 pm

Following up from my last message.
When going to https://drive.google.com/drive/folders/0B7kYte_CAcVpQXY3TEdqT0M1S2M
Click on the document titled "Telomere Shortening and Telomerase"

Report

Bill Andrews 10 Mar '17 at 7:50 am

I'm impressed!!!! The article has been rewritten to address my previous comments. This may now be the best article I have ever read on the subject!!!
Good for you Eleanor!!!

Report

michelle 23 Jul '18 at 12:00 pm

Thank you for your information. I will begin my study on telomeres and its function in the human body.

Report

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