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THE ROLES OF TELOMERES AND TELOMERASE IN REPLICATION OF LINEAR DNA

TELOMERES:

The ends of the linear chromosomes are known as telomeres: repetitive sequences that code for no particular gene. These telomeres protect the important genes from being deleted as cells divide and as DNA strands shorten during replication.

In humans, a six base pair sequence, TTAGGG, is repeated 100 to 1000 times. After each round of DNA replication, some telomeric sequences are lost at the 5′ end of the newly synthesized strand on each daughter DNA, but because these are noncoding sequences, their loss does not adversely affect the cell. However, even these sequences are not unlimited. After sufficient rounds of replication, all the telomeric repeats are lost, and the DNA risks losing coding sequences with subsequent rounds.

The discovery of the enzyme telomerase helped in the understanding of how chromosome ends are maintained. The telomerase enzyme attaches to the end of a chromosome and contains a catalytic part and a built-in RNA template. Telomerase adds complementary RNA bases to the 3′ end of the DNA strand. Once the 3′ end of the lagging strand template is sufficiently elongated, DNA polymerase adds the complementary nucleotides to the ends of the chromosomes; thus, the ends of the chromosomes are replicated.

TELOMERASE:

Telomerase, also called terminal transferase,[[1]](https://en.wikipedia.org/wiki/Telomerase#cite_note-1) is a ribonucleoprotein that adds a species-dependent telomere repeat sequence to the [3'](https://en.wikipedia.org/wiki/Directionality_%28molecular_biology%29#3.27-end) end of [telomeres](https://en.wikipedia.org/wiki/Telomere). A telomere is a region of repetitive [sequences](https://en.wikipedia.org/wiki/Sequence_%28biology%29) at each end of [eukaryotic](https://en.wikipedia.org/wiki/Eukaryote) [chromosomes](https://en.wikipedia.org/wiki/Chromosome) in most [eukaryotes](https://en.wikipedia.org/wiki/Eukaryote). Telomeres protect the end of the chromosome from [DNA damage](https://en.wikipedia.org/wiki/DNA_damage_%28naturally_occurring%29) or from fusion with neighbouring chromosomes. The fruit fly [*Drosophila melanogaster*](https://en.wikipedia.org/wiki/Drosophila_melanogaster) lacks telomerase, but instead uses [retrotransposons](https://en.wikipedia.org/wiki/Retrotransposon) to maintain telomeres.[[2]](https://en.wikipedia.org/wiki/Telomerase#cite_note-pmid21821789-2)

Telomerase is a [reverse transcriptase](https://en.wikipedia.org/wiki/Reverse_transcriptase) [enzyme](https://en.wikipedia.org/wiki/Enzyme) that carries its own [RNA molecule](https://en.wikipedia.org/wiki/Telomerase_RNA_component) (e.g., with the sequence 3′-[C](https://en.wikipedia.org/wiki/Cytosine)CC[A](https://en.wikipedia.org/wiki/Adenine)A[U](https://en.wikipedia.org/wiki/Uracil)CCC-5′ in [*Trypanosoma brucei*](https://en.wikipedia.org/wiki/Trypanosoma_brucei))[[3]](https://en.wikipedia.org/wiki/Telomerase#cite_note-pmid10097086-3) which is used as a template when it elongates telomeres. Telomerase is active in [gametes](https://en.wikipedia.org/wiki/Gamete) and most [cancer](https://en.wikipedia.org/wiki/Cancer) cells, but is normally absent from, or at very low levels in, most [somatic cells](https://en.wikipedia.org/wiki/Somatic_cell).

Telomerase is the enzyme responsible for maintenance of the length of telomeres by addition of guanine-rich repetitive sequences. Telomerase activity is exhibited in gametes and stem and tumor cells. In human somatic cells proliferation potential is strictly limited and senescence follows approximately 50-70 cell divisions. In most tumor cells, on the contrary, replication potential is unlimited. The key role in this process of the system of the telomere length maintenance with involvement of telomerase is still poorly studied. No doubt, DNA polymerase is not capable to completely copy DNA at the very ends of chromosomes; therefore, approximately 50 nucleotides are lost during each cell cycle, which results in gradual telomere length shortening. Critically short telomeres cause senescence, following crisis, and cell death. However, in tumor cells the system of telomere length maintenance is activated. Besides catalytic telomere elongation, independent telomerase functions can be also involved in cell cycle regulation. Inhibition of the telomerase catalytic function and resulting cessation of telomere length maintenance will help in restriction of tumor cell replication potential. On the other hand, formation of temporarily active enzyme via its intracellular activation or due to stimulation of expression of telomerase components will result in telomerase activation and telomere elongation that can be used for correction of degenerative changes.