Homework #5

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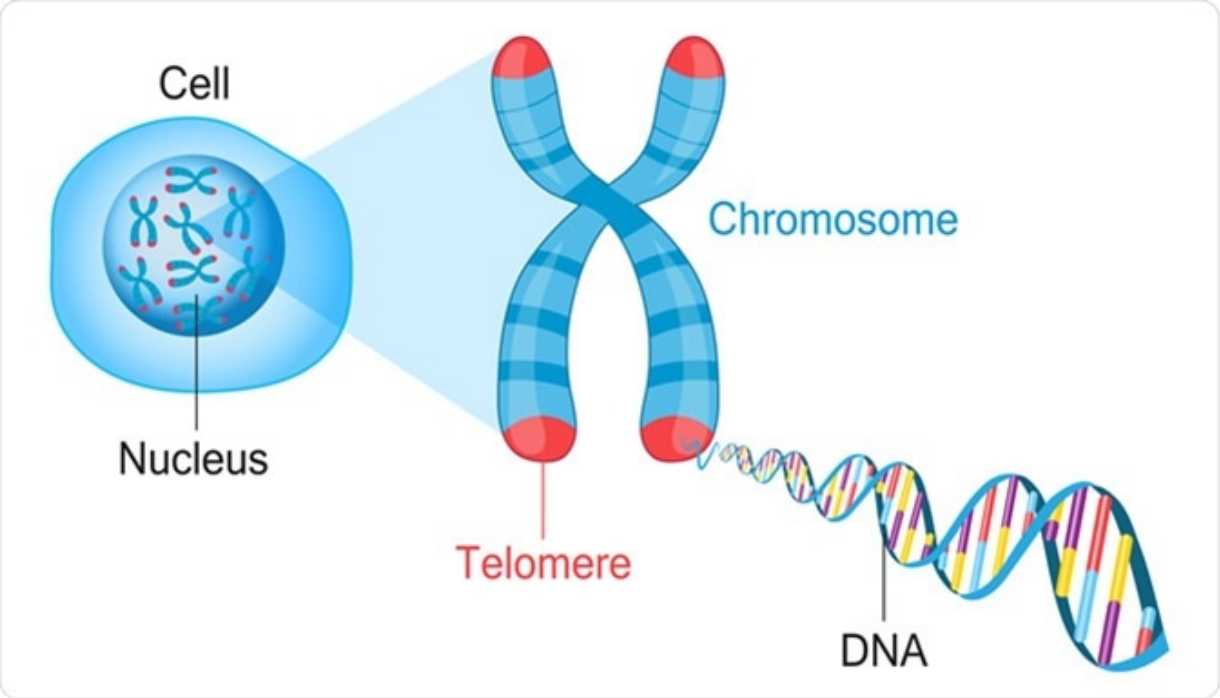
Context

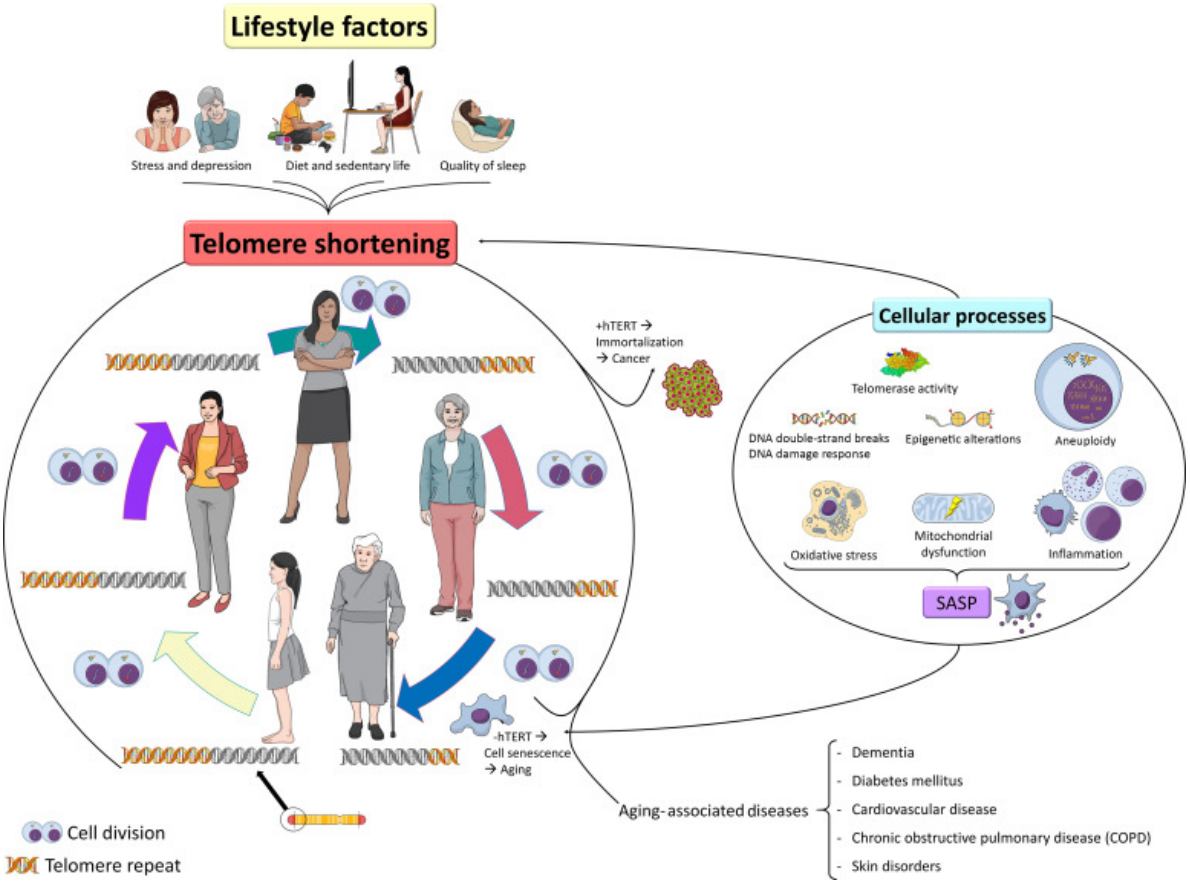


Telomeres are regions of chromosomes at their extremities. In essence, telomeres are part of chromosomes (which are composed of DNA) so telomeres are composed of DNA and other protein complexes. The DNA of which the telomeres are composed is repetitively composed of the TTAGGG nucleotides (which constitutes a hexamer - 6 nucleotides). In humans, the length of a telomer can range from 4,000 to 15,000 hexamers.

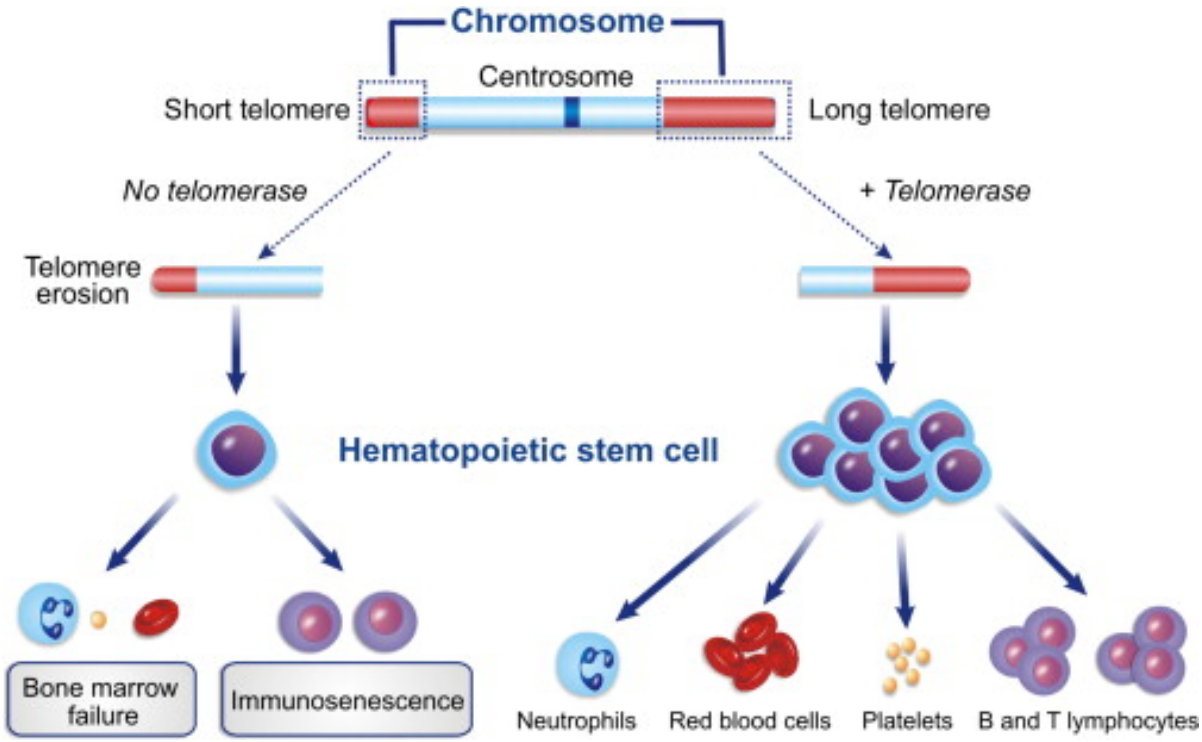
Telomeres have the role of sealing the ends of the chromosomes so that there is no danger of fusion of the genetic material, unwanted degradation or recombination of the genetic material from different chromosomes or the same chromosome. In this way, genetic stability, DNA conservation at replication and thus stability at mutations, especially in eukaryotes and prokaryotes with non-circular (linear) chromosomes are ensured. [1]

The process of telomerase in somatic cells and other cell types

Telomere length is associated with the aging process. The telomere length decreases at each cell division (ie, a series of telomere hexamers (TTAGGG) are lost). When the cell reaches a critical length of the telomeres then the cell will undergo the apoptosis process (death of the cell by programmed self-destruction). Exposure to various harmful factors can accelerate the shortening rate of telomeres, for example exposure to radiation or chemical factors.[2]



Stem cells, primary germ cells, lymphocytes, smooth muscle cells and fibroblasts and cancer cells are exceptions from the previous rule (during telomere cell division shortens) that is to say, to each cell division DNA replication is added to the chromosome ends compensating with division losses, thus preserving (approximately) the number of telomere hexamers, implicitly their length (Boccardi and Paolisso, 2014). This process is called telomerase, which is the regulation of the shortening rate of telomeres and is accomplished by activating the enzyme of the same name. This process is present in 85-90% of cancers (allowing cells to reproduce endlessly) and can be stopped with chemotherapy. In addition, telomerase inhibition processes may constitute cancer treatments by causing the cell to have shorter telomeres upon multiplication and eventually (after a series of divisions) to enter apoptosis. [3, 4]



Returning to somatic cells, they stop telomerase activity after birth (those that suffer from the process of losing hexamers during cell division). Short telomeres have been shown to be associated with cardiovascular disease, high blood pressure, diabetes, dementia and especially cancer (because short telomeres involve unstable chromosomes that may undergo genetic degradation, fusion, or recombination (ie, mutations). [2]

Pathologies associated with long telomeres

Normally telomere length will never increase. One of the reasons why telomere length will not increase is that the cell will spend far too much energy on its replication and thus its telomeres (Eisenberg, 2011). However, there are exceptions when telomere length may increase excessively leading to cancer or idiopathic pulmonary hypertension (Shen et al., 2013). [5]

DNA

DNA is a double-helical macromolecule (so two helices). Helices are made up of nucleotide chains (formed from heterocycle (nitrogenous base - purines (adenine and guanine), or pyrimidine bases (cytosine and thymine), in the case of thymine RNA is replaced by uracil), a pentose (sugar) and a or more phosphate groups). They are always grouped on opposite helices A with T and C with G, joined by hydrogen bridges. In addition, every 10 pairs of nuts are completely rotated.

DNA replication

At the time of the DNA replication process, the following happens: a series of enzymes break down the DNA molecule, by breaking the hydrogen bridges, into 2 helices. Then another series of proteins and enzymes associates both the right and left helixotide helix complementing the existing ones (A-T and C-G). The process takes place on short segments called Okazaki Fragments. The way of filling helices with neleotides is from $5\prime$ to $3\prime$, both on one end and on the other. In this way, two identical DNA molecules result.

Transcript in RNA

A gene (a DNA fragment that encodes a protein) is delimited by the promoter and terminator. Usually such portions (genes) are of interest when DNA is transcribed into RNA. This is accomplished with a series of enzymes that start from the promoter area and break the DNA molecule into two helices by breaking the hydrogen bridges on a portion. Then, on one of the helices, the transcript is completed: it is supplemented with complementary nucleotides this time by RNA (instead of T put uracil (U)) all the portion of the gene that is wanted to be cleaved. Thus the RNA molecule is obtained with gene information but in another format. After obtaining the RNA molecule, the piece of DNA that was broken is repaired by restoring the hydrogen bridges.

Protein translation

The translation of an RNA molecule (messenger RNA or mRNA) into a protein is performed with ribosomes. In principle, a ribosome consisted of large and small subunits. The large subunit has two transport RNA (A and P) binding sites (tRNAs) that transport specific amino acids for their anticodon (3 nucleotides complementary to a mRNA codon). The synthesis starts from AUG and then from 3 to 3 nuceotides (ie from codon to codon) binds

to the current polypeptide formed a new amino acid transported by the tRNA and which has the anticodon in correlation with the current codon in the mRNA. When a stop-codon is reached, the polypeptide is a protein and can be released.

Gel electrophoresis

Gel electrophoresis involves the separation of molecules based on their size (because larger molecules will move slower than smaller molecules that will move slower). This is done in a thin state of gel type material. When a current is applied to the jealous material (electrodes are attached to each end of the material) the molecules move to the electrode whose charges are opposite. While the current is switched on, if a dye is applied, the motion of the molecules can be observed.

PCR

In the PCR (Polymerase chain reaction) technique, a DNA segment can be rapidly copied thousands of times in the laboratory. The mixture is heated to separate DNA helices (hydrogen bridges break) and then cooled. The DNA polymerase enzyme is complemented by the DNA helices resulting from heating and cooling. This will result in 2 new DNA segments. After 20 cycles, there will be 1,048,516 copies of the DNA molecule. A cycle lasts about 5 minutes.

Sanger sequencing

Sanger sequencing is a sequencing method (finding the order of the nucleotides in a DNA sequence) which consists of the selective incorporation of di-deoxynucleotides (OH missing at the $3\prime$ end being replaced by H_2) in the course of DNA replication in vitro. Thus, to stop the complementarity process of the entire DNA molecule at a certain sequence (the non-neotide date at which the A, T, C or G stop is desired). In this way, molecules of different sizes are obtained. Using the electrophoresis on the 4 mixtures (ending in A, C, G or T) the order of the nucleotides in a DNA segment can be obtained. For this sequencing method, it is necessary to know the nuceotide primers that will be the primer for DNA polymerase (the starting point).

CRISPR-CAS9

Very briefly, from the earliest times until now there is a continuous battle between bacteria and viruses. Bacteria have developed a very interesting antivirus system over time. That is, in their genetic code they inserted viral DNA (their own genetic archive of the bacterium called CRISPR). When a virus attacks such a bacterium, the bacterium will generate an RNA copy of the viral genome and pass it on to the Cas9 protein that will search inside the bacterium for viral DNA that matches the viral RNA generated by the bacterium. When such a match is found, the protein will cut the DNA of the virus making it harmless. In addition CRISPR is programmable, meaning that Cas9 protein can be given any RNA and it will search for matching to cut DNA sequences at specific locations. This works for all living cells.

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