TELOMERE SHORTENING AS A MECHANISM FOR THE INDUCTION OF NEURODEGENETATIVE DISEASES

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Background. Telomeres are considered the "cellular biological clock" because their length could determine the possible number of cell divisions. Telomerase plays a role in maintaining telomere length. Telomerase ensures *de novo* addition of nitrogenous base sequences such as TTAGGG at the 3' end, protecting the chromosome end from double-strand breaks and preventing the DNA damage response (DDR).
Objective of the study. Identifying the mechanisms by which the progressive shortening of telomeres in nerve cells activates processes leading to neuronal senescence, with the aim of improving diagnosis and developing effective treatment methods.
Materials and Methods. To achieve the proposed objective, a literature review was conducted using 10 bibliographic sources from electronic libraries such as PubMed, MedScape, Hindawi, and ScienceDirect.
Results. Telomerase is active in young neural cells or neural precursor cells, but as they differentiate into mature neurons, its activity progressively decreases, affecting neuronal differentiation and stopping neurogenesis. In the absence of telomerase, telomere shortening can reach critical lengths, triggering a DDR-type response. This process induces the activation of ataxia-telangiectasia mutated kinase and other signaling proteins such as p53 and p21. The p53 protein plays a role in halting the cell cycle by activating p21, which inhibits cyclin-dependent kinase 2 and blocks the phosphorylation of the retinoblastoma protein (Rb). Hypophosphorylated Rb blocks E2 factor, a transcription factor, preventing the expression of genes necessary for cell division and causing cell cycle arrest in the G1 phase, leading to replicative senescence. Senescent cells secrete a senescence-associated secretory phenotype, which contributes to chronic inflammation and the spread of senescence in neighboring tissues. Chronic inflammation accelerates the accumulation of toxic proteins, such as beta-amyloid in Alzheimer's or alpha-synuclein in Parkinson's, promoting neuronal death and disease progression.
Conclusion: Telomere shortening in nerve cells induces senescence and chronic inflammation, accelerating neurodegeneration in diseases such as Alzheimer's and Parkinson's. Future therapies could aim at controlled activation of telomerase, the use of senolytic cells to eliminate senescent cells, and blocking senescence-associated secretory phenotype to reduce inflammation. These approaches could help slow down the neurodegenerative process and contribute to the development of more effective treatments.
Keywords: telomeres, telomerase, neurodegeneration, senescence.