

# Telomere Extension using CRISPR CAS9 for Age Associated Diseases and Longevity of Organism

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## Introduction

Telomere abrasion is considered a seal of the ageing process [1]. Significant progresses have been made in understating the basic biology of telomere function through in vitro research, the rendition of this research to an in vivo perspective is limited. Though numerous techniques are there to label telomeres, most of these are toxic to cells and cause DNA damage or non-compatible for in vivo applications[2]. The CRISPR-Cas system has enabled the refinement of these regions by fusing Cas9 to a fluorescent protein, allowing telomeres to be visualised in living organism [3]. The success rate of CRISPR Cas 9 technique is a new promise for future genome editing therapeutics. Telomere length and rate of telomere shortening are directly related to aging and eventual death for any organism. This effect can potentially be reversed by increasing the telomere length of an organism. CRISPR Cas system is an effective tool that can be used in the insertion of telomeres in the DNA of any given organism without error[4].

Previous methods of telomere elongation using modified mRNA encoding TERT has given results supporting the hypothesis that telomere elongation can increase the biological age of any organism [5]. Telomere extension using CRISPR Cas9 could potentially solve the end replication problem in human beings and cure aging and age-related problems that arise due to telomere shortening.

Telomere removal through the use of CRISPR Cas9 has already been experimentally conducted on Bone Marrow Neuroblasts cells, the results were that the removal of telomere led to cellular changes mainly a loss of mitochondrial function and an aggregation of Parkinson disease-associated proteins [6]. This study helped to understand how a specific process contributed to cell aging and has the potential to develop a model for both aging and population doubling in cells. As Telomeres can be completely removed through the use of CRISPR we can also add telomere using the same method by providing a Donor DNA consisting of n-number (example:1-2kb) of Telomere hexamers without the risk of insertional mutagenesis. Through this, telomeres can be added to all 23 pairs of chromosomes in human.

The addition of telomeres could also potentially delay the onset of age-related diseases such as dementia and could in theory reverse the effects of aging on human tissues. Experiments to increase the Telomere length have been conducted on human cell line and its results support this argument, these experiments were conducted using a modified mRNA encoding TERT [3].

As the function of Telomeres has been conserved across different species, we can also potentially increase the lifespan of other species by increasing the telomere length of an organism's DNA [7]. Telomerase editing is also possible by targeting the promoter of hTERT the CRISPR Cas system can be used to

both ablate and enhance TERT expression. This can help in cell apoptosis in tumor cells or could potentially turn normal cells into immortal cells depending on its design and utility[8].

If we map the genome of a young man and same human being after 10 years, the loss of telomeres in those 10 years can be calculated and the difference of telomere length can be added back along with the correction of any DNA damage that may have occurred in those 10 years, it should reverse the biological age of that human being rectifying all age related problems.

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**Received** 05 July, 2021; **Accepted** 19 July, 2021; **Published** 26 July, 2021

**How to cite this article:** Doshi C, "Divyashree MS. Telomere Extension using CRISPR CAS9 for Age Associated Diseases and Longevity of Organism". *Mol Biol* 10 (2021): 292.