



Mini Rewiew

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Is Telomere Shortening a Genetic Factor That Predisposes to



Diabetes Mellitus 2 and Oxidative Stress, or do They Induce It? A Telomere Shortening Predisposes to T2DM

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Abstract

Telomeres are structures at the ends of eukaryotic chromosomes and consist of tandemly repeated DNA sequences. Telomeres shorten with each cell division, and it is well known that telomere length in peripheral blood mononuclear cells (PBMCs) decreases with age. High oxidative stress can lead to accelerated telomere shortening, which causes premature cell senescence. In summary, this review shows the short Telomere Length has been identified in a limited number of population studies as a risk factor for development of T2DM. Also, it is importantly to notice the antioxidant properties of Curcumin which may play a key role in the prevention and treatment of premature aging while preserving the length of the telomeres.

Keywords: Telomere shortening; Oxidative stress; Genetic factor; Diabetes mellitus 2

Abbreviations: T2DM: Diabetes Mellitus 2; PBMCs: Cryopreserved Human Peripheral Blood Mononuclear Cells; WBCs: White Blood Cells; NO: Nitric Oxide; TBARS: Thiobarbituric Acid Reactive Substances.

Introduction

Diabetes mellitus 2 and telomere shortening

Diabetes Mellitus 2 (T2DM) is a multifactorial complex disorder which is emerging as a major cause of morbidity and mortality [1]. Telomeres are structures located at the extreme ends of chromosomes and are considered as indicators of biological age [2]. Increased telomere shortening has been demonstrated in several diseases, including diabetes type [3-6]. Telomere shortening increases with the diabetes duration, in our study, we established the potential importance of telomere dynamics in T2DM. We associated the time of disease duration closely in parallel to the progressive increased of inflammation and/or oxidative stress and both played a direct role in telomere shortening [7]. However, a study based on Chinese population found no relationship between Telomere Length and either the onset time or the Diabetes Mellitus 2 duration [8]. Genetic regulation of telomere could potentially explain telomere

shortening and also an increased risk for Diabetes Mellitus 2. Zee et al. [9], analyzed 11 telomere pathway genes and their relationship to the development of Diabetes Mellitus 2. A total of eleven tSNPs within TERF1, TNKS, TEP1, ACD and TERF2 were associated with Diabetes Mellitus 2 risk [9]. These findings suggest that genetic variation within the telomere pathway gene loci examined may be a useful predictor for Diabetes Mellitus 2 risk assessment [10,11]. Paik JK, et al. [12], did not observe an association between the selected TL-related SNPs and the presence of Hypertension and Coronary Heart Disease in [12]. These findings tell us the great importance of telomere dynamics in T2DM and the need for translational research.

Discussion

Oxidative stress and Telomere Length

Endogenous factors that cause telomere shortening are aging inflammation and oxidative stress. Telomere attrition

(expressed in WBCs) can serve as a biomarker of the cumulative oxidative stress and inflammation [13,14]. The association of UCP2 gene involved in the production of reactive oxygen species and functional promoter variant in mitochondria with the telomere length implies a link between mitochondrial production of reactive oxygen species and shorter telomere length in Diabetes Mellitus 2 [15]. Oxidative stress exerts a major influence on telomere dynamics by two principal mechanisms; firstly, the GGG triples on the telomere sequence are highly sensitive to the hydroxyl radical. Masi et al. [16] demonstrated that antioxidant defenses are important to maintain telomere integrity, potentially reducing the progression of vascular ageing in patients with T2DM. Secondly in contrast to genomic DNA, telomeric DNA was reported to be deficient in the repair of single-strand breaks. Consequently telomeres appear to be especially vulnerable to the accumulation of ROS-induced DNAstrand breaks [17,18].

Prospective treatment for diabetes mellitus 2

Recent studies propose that telomere shortening and abnormal telomerase activity occur in patients with diabetes mellitus 2 and targeting the telomere-telomerase system has become a prospective treatment for diabetes mellitus [19]. Dietary supplementation of antioxidants has been proposed as alternative treatment to reduce oxidative stress caused by obesity and diabetes. Different studies have shown that curcumin has antioxidant and antihyperglycemic properties in diabetes and obese animal models [20-24]. Hyperglycemia modifies oxygen consumption rate, NO synthesis and increases TBARS levels in mitochondria from the liver and kidneys of diabetic mice, whereas curcumin may has a protective role against these alteration [25-27]. Antioxidant properties of curcumin could play a key role in the prevention and treatment of chronic inflammation diseases [28]. Zhou et al. [29] demonstrated that diet ingredients significantly have an impact on inflammation and oxidative stress markers, which probably also have an effect on Telomere Length. Diabetes patients with normal plasma glucose levels had longer Telomere Length [29].

Conclusion

Telomere Length has been identified in a limited number of population studies as a risk factor for development of T2DM, antioxidant defences are important to maintain telomere integrity, Curcumin which may play a key role in the prevention and treatment of premature aging while preserving the length of the telomeres.

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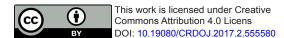
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