Hypothesis

Telomere shortening occurs in patients with ectodermal dysplasia

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ABSTRACT

Ectodermal Dysplasia (ED) is a rare congenital disorder that is characterized by sparse hair, lack or absence of sweat glands, and rod-shaped teeth, which are diagnosed by two or three of these features. There are approximately 200 subtypes of ED have been identified. One of the rare and severe subtypes of ED is Dyskeratosis Congenita (DC). A mutation in the telomere-maintain genes causes this disorder. Since this rare disorder is a subset of ED disease, this study aimed to examine telomeres in these patients and expect to see telomere shortening in ED patients.

***Keywords*:** Ectodermal Dysplasia, telomere shortening, telomere length, Dyskeratosis Congenita

INTRODUCTION

Ectodermal Dysplasia (ED) is a rare heterogeneous genetic disorder. The estimated national prevalence is 1 per 100,000 live births [1]. Hereditary patterns of Ectodermal Dysplasia include Autosomal Dominant (AD), Autosomal Recessive (AR), and X-Link Recessive (XLR), so it affects men and women equally. Ectodermal

dysplasia can occur due to mutations in genes encoding fetal ectoderm [2]. The diagnostic triangle is spare hair, decrease, or lack of sweat glands and rod-shaped teeth [3]. Almost 200 different ED subtypes have been identified, and about 200 genes were involved [4]. One ED phenotype is Dyskeratosis Congenita (DC). The prevalence of approximately 1 per 1,000,000 persons. Mutations in telomere biology genes have been identified as DC-specific cause and telomere shortening [5]. There are several ways to evaluate telomere shortening and size measurement in ectodermal dysplasia patients (Table 1) [6–8]. One of the cost-effective and fast method is to use the Real-time Polymerase Chain Reaction (real-time PCR) technique. In this method, the Telomere-Size (T/S) ratio is used in the patient and control samples. Telomere can be measured by comparing rates and examination information. Since the distinction within the telomeres measure is statically inspected in this strategy, it will be caught on the shortness is noteworthy (Figure1) [9].

Table 1. Comparisons of different TL measurement methods [7,8]

Method	Advantage	limitation
TRF	Common method for research Gold standard common method for research	larger amounts of starting DNA required Labor intensive Subtelomeric polymorphisms can impact data
Q-PCR **MMqPCR**	Can use small amounts of DNA many population-based studies for comparisons Referenced to standard single copy gene	Requires qPCR equipment large variations among different laboratories Reference standards lacking
Q-FISH	Assess telomere lengths in specific cell types identify single telomere changes	Labour intensive TLs expressed as relative fluorescence units (often compared to standard centromeric value)
STELA	Does not require viable cells detect the shortest telomeres Does not require specialized equipment	Labour intensive low throughput Does not recognize ends lacking a telomere
TeSLA	Automatic quantitation of telomere sizes works on many animal types	low throughput Labour intensive
PRINS	Identify single telomere changes assess telomere lengths in specific cell types	Labour intensive Requires microscope Requires mitotically active cells for metaphase chromosomes

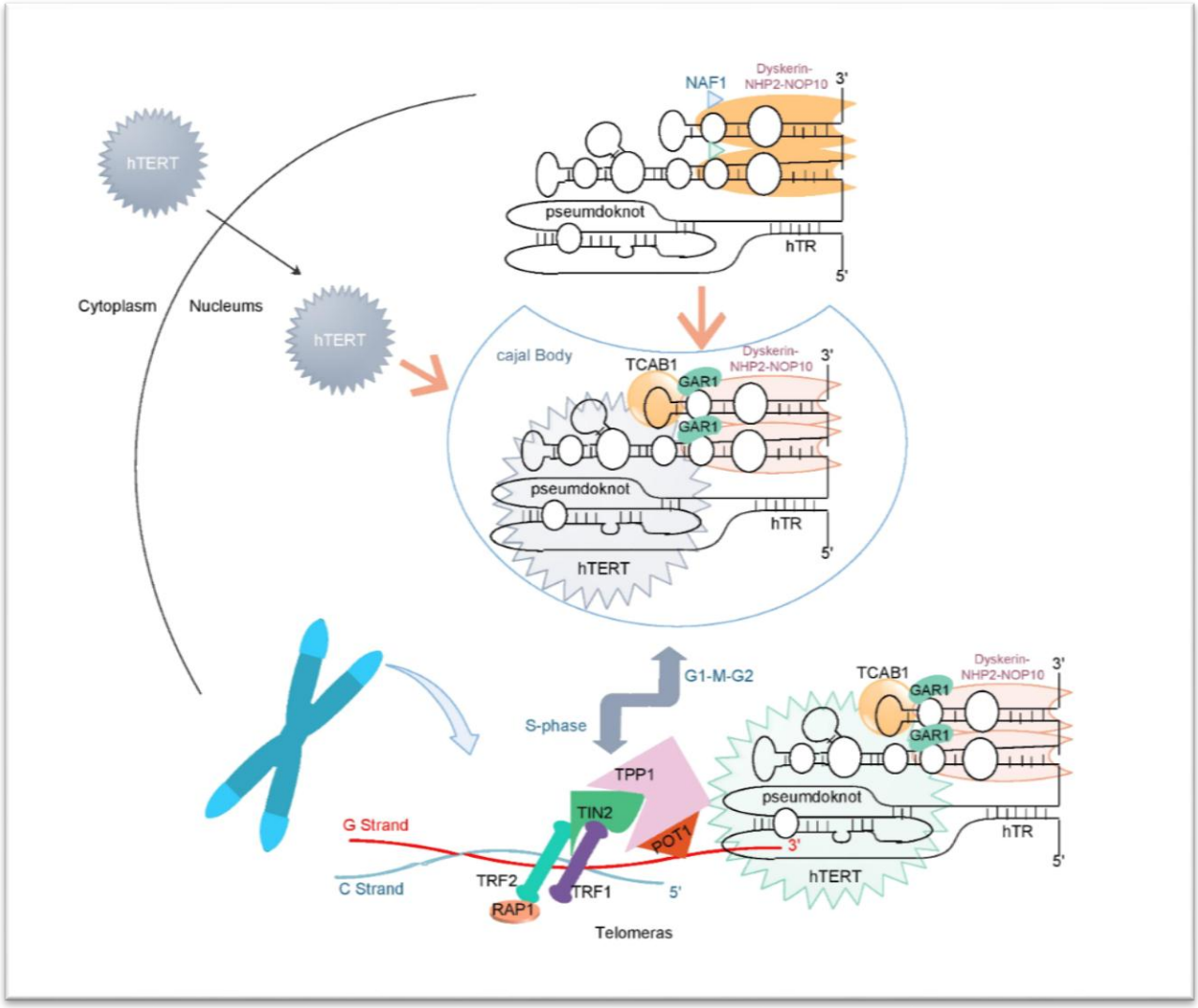

Figure 1. Telomerase assembly and recruitment to telomeres. TERT after being synthesized in the cytoplasm, enters the nucleus with the chaperones. TR is made in the nucleus but is not expressed because it is a non-coding RNA. TR has different domains to which NOP10, NHP2, Dyskerin, and GAR1 proteins bind and form the TERC complex. TERT and TERC are then entered into CB by TCAB1. In CB, telomerase is formed and matures. In S phase of the cell cycle for telomere lengthening, telomerase recruited to telomere by TPP1 Shelterin complex (the shelterin complex consists of TPP1, POT1, TRF1, TRF2, TIN2, Rap1 proteins). Telomerase, along with the shelterin, adds TTAGGG repetitions to the telomere. Once the telomere length is sufficient, the negative feedback generated by the POT1, disables the telomerase and re-enters the CB.

This theory points to recommend the assessment of the estimate of the telomere in ED patients. Anna Marrone appeared telomere shortening and telomerase in Dyskeratosis Congenital patients. Dyskerin and TERC were related in the telomerase complex, and DC has been identified as a telomerase deficiency disorder characterized by short telomeres. They showed that mutations in the gene disrupt this connection [10]. Xi-Lei Zeng *et al*, found that the deformity in telomere homeostasis in X-DC is diminishing within the steady state Telomerase RNA (TER) [11]. According to studies, therefore, we expect to see telomere shortening in patients with ectodermal dysplasia. Since DC is a subtype of ED and telomere shortening has been assessed in these patients; therefore, we decided to present this hypothesis to do in Ectodermal Dysplasia patients, which has not been studied so far. This hypothesis may improve ED patient's management. Because telomere shortening has a severe effect on patients phenotype, by presenting this hypothesis and doing it in the future, one of the criteria for genetic counseling for patients with Ectodermal Dysplasia should be considered.

CONCLUSION

Ectodermal Dysplasia is a heterogeneous abnormality. Because the disorder has many subtypes, dyskeratosis congenita is one of its rarest subtypes. Telomere shortening is a common cause in this rare type. Therefore, we hypothesized that when telomere shortening occurs in the subtype of Ectodermal Dysplasia, it occurs in the Ectodermal patients.

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