TERC gene

telomerase RNA component

Normal Function

The *TERC* gene provides instructions for making one component of an enzyme called telomerase. Telomerase maintains structures called telomeres, which are composed of repeated segments of DNA found at the ends of chromosomes. Telomeres protect chromosomes from abnormally sticking together or breaking down (degrading). In most cells, telomeres become progressively shorter as the cell divides. After a certain number of cell divisions, the telomeres become so short that they trigger the cell to stop dividing or to self-destruct (undergo apoptosis). Telomerase counteracts the shortening of telomeres by adding small repeated segments of DNA to the ends of chromosomes each time the cell divides.

In most types of cells, telomerase is either undetectable or active at very low levels. However, telomerase is highly active in cells that divide rapidly, such as cells that line the lungs and gastrointestinal tract, cells in bone marrow, and cells of the developing fetus. Telomerase allows these cells to divide many times without becoming damaged or undergoing apoptosis. Telomerase is also abnormally active in cancer cells, which grow and divide without control or order.

The telomerase enzyme consists of two major components that work together. The component produced from the *TERC* gene is known as hTR. The hTR component is an RNA molecule, a chemical cousin of DNA. It provides a template for creating the repeated sequence of DNA that telomerase adds to the ends of chromosomes. The other major component of telomerase, which is produced from a gene called *TERT*, is known as hTERT. The function of hTERT is to add the new DNA segment to chromosome ends.

Health Conditions Related to Genetic Changes

Dyskeratosis congenita

At least 20 mutations in the *TERC* gene have been identified in people with dyskeratosis congenita. This disorder is characterized by changes in skin coloring (pigmentation), white patches inside the mouth (oral leukoplakia), and abnormally formed fingernails and toenails (nail dystrophy). People with dyskeratosis congenita have an increased risk of developing several life-threatening conditions, including

cancer and a progressive lung disease called pulmonary fibrosis. Many affected individuals also develop a serious condition called aplastic anemia, also known as bone marrow failure, which occurs when the bone marrow does not produce enough new blood cells.

Some of the *TERC* gene mutations that cause dyskeratosis congenita result in an absent or unstable hTR molecule; others change the way hTR interacts with hTERT or other components of the telomerase enzyme.

TERC gene mutations lead to telomerase dysfunction, impaired maintenance of telomeres, and reduced telomere length. Cells that divide rapidly are especially vulnerable to the effects of shortened telomeres. As a result, people with dyskeratosis congenita may experience a variety of problems affecting quickly dividing cells in the body such as cells of the nail beds, hair follicles, skin, lining of the mouth (oral mucosa), and bone marrow.

Breakage and instability of chromosomes resulting from inadequate telomere maintenance may lead to genetic changes that allow cells to divide in an uncontrolled way, resulting in the development of cancer in some people with dyskeratosis congenita.

Idiopathic pulmonary fibrosis

Several mutations in the *TERC* gene have been identified in people with the progressive lung disease idiopathic pulmonary fibrosis. This condition causes scar tissue (fibrosis) to build up in the lungs, which makes the lungs unable to transport oxygen into the bloodstream effectively. Mutations in the *TERC* gene have been found in cases that run in families (familial pulmonary fibrosis) and, less commonly, in isolated (sporadic) cases. Some individuals with idiopathic pulmonary fibrosis due to *TERC* gene mutations have family members with other features of dyskeratosis congenita (described above), such as aplastic anemia or cancer.

Mutations in the *TERC* gene reduce or eliminate the function of telomerase, which allows telomeres to become abnormally short as cells divide. The shortened telomeres likely trigger cells that divide rapidly, such as cells that line the inside of the lungs, to stop dividing or to die prematurely. In people with idiopathic pulmonary fibrosis, shorter telomeres are associated with a more severe disease and a quicker decline in lung function. Additional research is needed to confirm how shortened telomeres contribute to the progressive scarring and lung damage characteristic of idiopathic pulmonary fibrosis.

Idiopathic pulmonary fibrosis is a complex disease that is probably caused by a combination of genetic and environmental factors. Studies suggest that many affected people with *TERC* gene mutations may have also been exposed to environmental risk factors, such as cigarette smoke or certain kinds of dust or fumes. It is possible that mutations in the *TERC* gene increase a person's risk of developing idiopathic pulmonary fibrosis, and then exposure to certain environmental factors can trigger the disease.

Other disorders

TERC gene mutations have also been found in people with isolated aplastic anemia, a form of bone marrow failure that occurs without the other physical features of dyskeratosis congenita (described above). Researchers suggest that mutations affecting different parts of the telomerase enzyme may account for the absence of these features. Some believe that isolated aplastic anemia caused by *TERC* gene mutations may actually represent a late-onset form of dyskeratosis congenita in which physical features such as nail dystrophy are mild and may not be noticeable.

Other Names for This Gene

- hTERC
- hTR
- SCARNA19
- small Cajal body-specific RNA 19
- telomerase RNA
- telomerase RNA component gene
- TR
- TRC3

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of TERC (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7012[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28TERC%5BTIAB%5D%29+OR+%28telomerase+RNA+component%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- TELOMERASE RNA COMPONENT; TERC (https://omim.org/entry/602322)
- PULMONARY FIBROSIS AND/OR BONE MARROW FAILURE SYNDROME, TELOMERE-RELATED, 2; PFBMFT2 (https://omim.org/entry/614743)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7012)

- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=TERC[gene])

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Genomic Location

The *TERC* gene is found on chromosome 3 (https://medlineplus.gov/genetics/chromosome/3/).

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