Research paper on telomerase

Health & Medicine, Cancer

Telomerase also known as telomere terminal transferase is a type enzyme in all vertebrates that extends Die ribonucleic acid sequence by repeating TTAGGG to the Die ribonucleic acid terminal strands in the region known as the telomere. It is found in adult germ cells, fetal tissues, and tumor cells. Telomere is the region of repeated nucleotide, which is made up of non-coding Die ribonucleic acid material. The region prevents loss of vital Die ribonucleic acid from chromosome terminals. This results to only a hundred to two hundred nucleotides being lost each interval the chromosome is duplicates, thus no damage is caused to the living organism's Die ribonucleic acid. TERA is an abbreviation used in reference to telomerase that has its Ribonucleic acid cells. The Ribonucleic acid molecule is used as an overlay in the elongation process of telomeres.

The elongated telomerase is usually shortened after every replication cycle. As mentioned earlier, telomeres are the structures at the end of chromosomes characterized by a repetition of tandem of the TTAGGG nucleotide sequence. Studies show that, at every passing stage of an organism’s life, these sequences of nucleotides gradually shorten during every process of cell division and replication. This makes the length of the telomere face gradual decline after every replication cycle. The shortening of the telomere consequently causes cellular damage being that it is unable of undergoing self-duplication (Mattson 39). This leads to a sequence of events, from gradual progressive cellular dysfunction to aging phenomena, which eventually leads to death.

Facts about Telomerase

The responsibility of enzyme telomerase is to maintain the integrity of the telomeres. Chromosomes being crucial part of all life's functions, and an integral part of the living organism, its systems are maintained in aspects relating to its positioning, accuracy, and structural integrity of the telomeres. By addition of multiple repeats of nucleotides to the telomeres, the enzyme telomerase acts to prevent the loosing of genetic information and damaging DNA during replication. The conclusion arrived at by scientist is that, telomerase is the main hormone that assists in replacing telomere sequences and genetic repair, thus the clock that controls the life span of the replicating cells are re-rearranged. Alexey Olovnikov, a Soviet biologist, was the first to predict the existence telomerase mechanism or the compensatory shortening of telomere in 1973. He also gave the suggestion on the supposed explanation of telomere on aging, and the connections of telomere to cancer. The enzyme telomerase was a discovery of Elizabeth Blackburn and Carol W. Greider in 1984.

Structure of Telomerase

Dr. Cohen Scott in 2007 identified that, the human telomerase was composition of protein. He found out that the telomerase was made up of dual molecules, each of human dyskerin, TERT, and telomerase Ribonucleic acid. The genes of telomerase subunits include TERC, TEP1, TERT, and DKC1 etc, and are located on the different chromosomes in human genome. Human TERT gene (hTERT) is translated into amino acids of 1132 amino acids. Sequencing is done for TERT amino acids/proteins from many eukaryotes. Telomerase reverse transcriptase, peptide consisting of two or

more amino acids, folds with telomerase ribonucleic acid, a non-coding RNA that is 451 nucleotides long in man. Telomerase reverse transcriptase has a protective cover like structure that enables it to wrap itself on the chromosome to add mono-stranded telomere repeats. Telomerase reverse transcriptase is a reverse RNA polymerase, and is a type of enzyme using mono-stranded Ribonucleic acid as an overlay to create mono-stranded Die-ribonucleic acid.

Not being specific, this class of enzyme, Telomerase reverse transcriptase, is isolated from viruses that are used by scientists and researchers in the biological and molecular process of the enzyme reverse transcriptase. This allows Ribonucleic acid as to as an overlay to create a number of Die ribonucleic acid duplicates of a sequence target (Theimer & Feigon 310). Telomerase reverse transcriptase has its own over layer, Telomerase ribonucleic acid. Emmanuel Skordalakes and his team at The Wistar Institute in Philadelphia decoded the amino acids structure of high-resolution protein speed up subunit of Telomerase reverse transcriptase in 2008. The structure showed that the amino acid has 4 conserved domains fingers, Ribonucleic acid, palm, Binding Domain (TRBD) and thumb that are arranged into a circular configuration sharing common characteristics with retroviral reverse bacterio-phage B-family Die ribonucleic acid polymerases, viral Ribonucleic acid polymerases, and transcriptases.

Functions and Mechanism of Telomerase

Telomerase activities come under regulation during development and have a very low to almost undetectable activity in body cells. Their main function in

the body is to bind the first few nucleotides of the template to the last telomere sequence on the chromosome. They add a new telomere repeats (5'-GGTTAG-3') sequence, let go, realign the new 3'-end of telomere to the template, and repeat the process.

Telomerase reverse transcriptase can add a 6 nucleotide recurring sequence, that is, 5'-TTAGGG to 3'chromosomal strand, when used by Telomerase RNA. The TTAGGG repeats are referred to as telomeres. The layover region of Telomerase RNA is 3'-CAAUCCCAAUC-5'. The first TER structures of telomerase have been reported to be active in regions of the catalytically essential pseudo knot and CR4/CR5 domains of human TER (Gillis & Schuller 635). It provides a structural basis for interpreting biochemical data and mutational.

Uses and Applications of telomerase

The enzyme has found a widespread use and application in various clinical issues such as the ones discussed below.

Application in Aging

Replacement of Die ribonucleic acid’s short bits, known as telomeres is allowed by the enzyme telomerase. The process is otherwise shortened when mitotic cell division occurs. If dividing cells divide recursively in normal occurrences, without telomerase being present, all off springs will attain their Hay-flick limit at some point. Each cell that divides can replace lost bit of Die ribonucleic acid, and any individual cell that promotes aging can also divide when unbounded with the presence of telomerase. Unbounded growth is a real crucial step in enabling cancerous development and growth. Many

researchers are excited with this unbounded growth property, but caution is advised in exploitation of this unique property, being that it is found in same embryonic-stem cells, which permits repeated cell division, and forms a person. Telomerase is manifested in cells that require regular division in adults. Somatic cells manifest it at only very reduced levels in a cell cycle supported approach (Cohen, Graham, Lovrecz, Bache and Robinson 1852). The ability of telomerase to reactivate reversed tissue degeneration, make if applicable in age treatment procedures, in clinics.

Application in Cancer Research

The time for biologically aging after maturity gets extension courtsey of the tumor suppressor Retinoblastoma amino acid and protein- TP53, is when cells are approaching the Hay flick limit in cell cultures. The altered cells ultimately undergo a process referred to as crisis where most of the cultured cells die. A cell sometimes never ceases division once it arrives at crisis. With every subsequent cell division in every aspects of typical cell division situation, the telomeres get lost, and the chromosomes' integrity declines. Chromosomes that are exposed are interpreted as being dual stranded splits in DNA. Repairing such damages is usually done by reattaching together the broken ends. During anaphase division of the cells, chromosomes that are fused randomly are separated apart, to cause many chromosomal abnormalities and mutations.

The continuity of this process leads to the genome of the cell becoming unstable. Considerable damage eventually will be done to the chromosome of the cell to the extent that cell undergoes mutation and finally dies.

Additional mutation triggers the action of telomerase (Lenhard 115). Some offspring and cells become immune to death; meaning that, regardless of the number, the cell undergoes divisions; their chromosomes will not become unstable. They bypass the Hay flick limit, and thus avoid death of the cell so long as their duplication conditions are maintained. This is possible with the activation of telomerase. The activity of telomerase allows some many carcinogenic cells' division last virtually forever, thus making them to be considered as immortal. This is why they are tumor forming.

Roles of Telomerase in cancer, life's quality, and heart ailments

Other roles and applications of telomerase include the up-regulation of seventy genes that are identified or synonymous in the spread and growth of cancer through the body, plus the glycolysis activation, which enables carcinogens to rapid consumption of glucose to assist their growth rate that is programmed. UCSF has exhibited works that show that women taking the care of their sick next of keen have shortened telomeres on reports that their emotional stress was at the highest point. Scientists also found the activity of telomerase at the blockage sites of in tissue of the heart artery. This might be the reason why coronary attacks may suddenly increase with age. Telomerase contributes to the growth and blockage development. In 2009, it was exposed that, the amount of telomerase activity is significantly increased by psychological stress. The activity of telomerase was examined in peripheral blood mononuclear cells. A 2010 study, found out that there was, significantly greater, telomerase activity in participants than controls samples in a three-month retreat on meditation. As per the 2007 study,

there was no correlation between telomere length and socio-economic status.

Role Telomerase in human diseases

In 2005, the mutations in Telomerase reverse transcriptases faced implications in predisposition of patients to diseases such as aplastic anemia, which is a condition where the bone marrow is incapable of producing blood cells, the syndrome Cri du chat is a disorder that involves the loosing of small parts of the chromosome 5 short arms. Dyskeratosis congenital is a bone marrow disease, which may be contributed by some mutations in telomerase subunits. In the DC cases, about 35 percent cases are X-linked-recessive on the DKC1 locus and 5 percent cases are autosomal dominant on the Telomerase reverse transcriptases and Telomerase RNA loci. Patients suffering from DC experience very painful bone marrow drawbacks such as nail dystrophy, leucoplakia, and abnormality in skin pigmentation, amongst other symptoms. People with either DKC1 or TERC mutations have defective telomerase and shorter telomeres activity than their age mates.

Reports that links of families having auto-somal dominant Dyskeratosis congenita to a heterozygous mutations in Telomerase reverse transcriptases, has been published. The patients having the symptoms, also exhibits increased rates of genetic anticipation and telomere shortening (Emily & Mariela103).

Target on Telomerase as a potential drug

The fact that a human’s immunity system faces difficulties in recognizing carcinogens, makes cancer a very difficult to fight. Telomerase being vital for

the persistence of numerous types of cancer, it is being targeted as a possible drug. The attempt to use a drug to stop telomerase in carcinogens, resumes the process of shortening of telomere. The length of telomerase will be reduced further by the continued cell division, and mutations continue to occur while the cell loses its stability. Experimental vaccine therapies and drugs targeting activities of telomerase have been tried in mice models, some vaccines are now in primary clinical trials. The research by Geron, involving telomerase vaccination and telomerase inhibition, is currently being clinically tried, to see its potential of being used as a drug. The recent approval by the researcher is of an IND as one type of the vaccines.

The platform for the vaccine and functionality is being tried together with Merck, with application of three different procedures. Dendritic cell vaccine was derived by the researcher Geron's embryo stem-cell to target telomerase and is now at the primary clinical trial stage. These trial vaccines attempt to help human immunity system to handle attack carcinogen that express telomerase. GRN163L, a drug that tries to inhibit telomerase from proliferation of cancer cell by inhibiting telomerase action, is the first achievement by Geron (Gagnon 154). Currently it is in separate primary stages of clinical trials.

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