Science News

from research organizations

Hidden secret of immortality enzyme telomerase

Can we stay young forever, or even recapture lost youth?

Date: February 27, 2018

Source: Arizona State University

Summary: Research has recently uncovered a crucial step in the telomerase enzyme catalytic cycle. This catalytic cycle determines the ability of the human telomerase enzyme to synthesize DNA.

Share:

RELATED TOPICS

Health & Medicine
- Stem Cells
- Human Biology
- Lymphoma
- Genes
- Healthy Aging
- Skin Cancer
- Prostate Cancer
- Immune System

RELATED TERMS
- Telomere
- Fertility
- Enzyme
- BRCA2
- DNA repair
- BRCA1
- Lactose intolerance
- Circadian rhythm

FULL STORY

Can we stay young forever, or even recapture lost youth?

Research from the laboratory of Professor Julian Chen in the School of Molecular Sciences at Arizona State University recently uncovered a crucial step in the telomerase enzyme catalytic cycle. This catalytic cycle determines the ability of the human telomerase enzyme to synthesize DNA "repeats" (specific DNA segments of six nucleotides) onto chromosome ends, and so afford immortality in cells. Understanding the underlying mechanism of telomerase action offers new avenues toward effective anti-aging therapeutics. Illustration depicting the enzyme telomerase This figure depicts the enzyme telomerase as well as telomeres relative to a chromosome.

Typical human cells are mortal and cannot forever renew themselves. As demonstrated by Leonard Hayflick a half-century ago, human cells have a limited replicative lifespan, with older cells reaching this limit sooner than younger cells. This "Hayflick limit" of cellular lifespan is directly related to the number of unique DNA repeats found at the ends of the genetic material-bearing chromosomes. These DNA repeats are part of the protective capping structures, termed "telomeres," which safeguard the ends of chromosomes from unwanted and unwarranted DNA rearrangements that destabilize the genome.

Each time the cell divides, the telomeric DNA shrinks and will eventually fail to secure the chromosome ends. This continuous reduction of telomere length functions as a "molecular clock" that counts down to the end of cell growth. The diminished ability for cells to grow is strongly associated with the aging process, with the reduced cell population directly contributing to weakness, illness, and organ failure.

The fountain of youth at molecular level

Counteracting the telomere shrinking process is the enzyme, telomerase, that uniquely holds the key to delaying or even reversing the cellular aging process. Telomerase offsets cellular aging by lengthening the telomeres, adding back lost DNA repeats to add time onto the molecular clock countdown, effectively extending the lifespan of the cell. Telomerase lengthens telomeres by repeatedly synthesizing very short DNA repeats of six nucleotides -- the building blocks of DNA -- with the sequence "GGTTAG" onto the chromosome ends from an RNA template located within the enzyme itself. However, the activity of the telomerase enzyme is insufficient to completely restore the lost telomeric DNA repeats, nor to stop cellular aging.

The gradual shrinking of telomeres negatively affects the replicative capacity of human adult stem cells, the cells that restore damaged tissues and/or replenish aging organs in our bodies. The activity of telomerase in adult stem cells merely slows down the countdown of the molecular clock and does not completely immortalize these cells. Therefore, adult stem cells become exhausted in aged individuals due to telomere length shortening that results in increased healing times and organ tissue degradation from inadequate cell populations.

Tapping the full potential of telomerase

Understanding the regulation and limitation of the telomerase enzyme holds the promise of reversing telomere shortening and cellular aging with the potential to extend human lifespan and improve the health and wellness of elderly individuals. Research from the laboratory of Chen and his colleagues, Yinnan Chen, Joshua Podlevsky and Dhenugen Logeswaran, recently uncovered a crucial step in the telomerase catalytic cycle that limits the ability of telomerase to synthesize telomeric DNA repeats onto chromosome ends.

"Telomerase has a built-in braking system to ensure precise synthesis of correct telomeric DNA repeats. This safe-guarding brake, however, also limits the overall activity of the telomerase enzyme," said Professor Chen. "Finding a way to properly release the brakes on the telomerase enzyme has the potential to restore the lost telomere length of adult stem cells and to even reverse cellular aging itself."

This intrinsic brake of telomerase refers to a pause signal, encoded within the RNA template of telomerase itself, for the enzyme to stop DNA synthesis at the end of the sequence 'GGTTAG'. When telomerase restarts DNA synthesis for the next DNA repeat, this pause signal is still active and limits DNA synthesis. Moreover, the revelation of the braking system finally solves the decades-old mystery of why a single, specific nucleotide stimulates telomerase activity. By specifically targeting the pause signal that prevents restarting DNA repeat synthesis, telomerase enzymatic function can be supercharged to better stave off telomere length reduction, with the potential to rejuvenate aging human adult stem cells.

Human diseases that include dyskeratosis congenita, aplastic anemia, and idiopathic pulmonary fibrosis have been genetically linked to mutations that negatively affect telomerase activity and/or accelerate the loss of telomere length. This accelerated telomere shortening closely resembles premature aging with increased organ deterioration and a shortened patient lifespan from critically insufficient cell populations. Increasing telomerase activity is the seemingly most promising means of treating these diseases.

While increased telomerase activity could bring youth to aging cells and cure premature aging-like diseases, too much of a good thing can be damaging for the individual. Just as youthful stem cells use telomerase to offset telomere length loss, cancer cells employ telomerase to maintain their aberrant and destructive growth. Augmenting and regulating telomerase function will have to be performed with precision, walking a narrow line between cell rejuvenation and a heightened risk for cancer development.

Distinct from human stem cells, somatic cells constitute the vast majority of the cells in the human body and lack telomerase activity. The telomerase deficiency of human somatic cells reduces the risk of cancer development, as telomerase fuels uncontrolled cancer cell growth. Therefore, drugs that increase telomerase activity indiscriminately in all cell types are not desired. Toward the goal of precisely augmenting telomerase activity selectively within adult stem cells, this discovery reveals the crucial step in telomerase catalytic cycle as an important new drug target. Small molecule drugs can be screened or designed to increase telomerase activity exclusively within stem cells for disease treatment as well as anti-aging therapies without increasing the risk of cancer.

Story Source:

Materials provided by **Arizona State University**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Chen, Y., J.D. Podlevsky, D. Logeswaran and J.J.-L. Chen. **A single nucleotide incorporation step limits human telomerase repeat addition activity**. *EMBO*, 2018 DOI: 10.15252/embj.201797953

Cite This Page: MLA | APA | Chicago

Arizona State University. "Hidden secret of immortality enzyme telomerase: Can we stay young forever, or even recapture lost youth?." ScienceDaily. ScienceDaily, 27 February 2018. <www.sciencedaily.com/releases/2018/02/180227142114.htm>.

RELATED STORIES

Two-Step Process Leads to Cell Immortalization and Cancer
Aug. 17, 2017 — Immortalization of cells is a necessary step in the development of cancer, and scientists think that the main cause is turning on an enzyme -- telomerase -- that lengthens chromosomal telomeres and ... read more »

Scientists Produce Clearest-Ever Images of Enzyme That Plays Key Roles in Aging, Cancer
Oct. 15, 2015 — The telomerase enzyme is known to play a significant role in aging and most cancers. Scientists have discovered several major new insights about this enzyme and they are now able to see the complex ... read more »

Study Reveals Key Structure in Telomerase Enzyme, a Target for Cancer Drugs
Oct. 5, 2015 — Researchers have determined the structure of a key part of the enzyme telomerase, which is active in most cancers and enables cancer cells to proliferate indefinitely. The new findings reveal how the ... read more »

Telomerase Can Be Successfully Targeted by a Highly Specific Inhibitor
Sep. 3, 2015 — New research shows exactly how a known, highly selective small molecule telomerase inhibitor is able to bind with the enzyme, thus opening the possibility of developing more telomerase inhibitors ... read more »

FROM AROUND THE WEB

Below are relevant articles that may interest you. ScienceDaily shares links with scholarly publications in the TrendMD network and earns revenue from third-party advertisers, where indicated.

Can plants tell us something about longevity?
Phys.org, 2019

Scientists unveil a hidden secret of the immortality enzyme telomerase
MedicalXpress

Resources for rheumatologists: re-thinking the role of pathogenic drivers in rheumatoid arthritis
Bristol-Myers Squibb, 2019

Researchers identify new potential target for cancer therapy
MedicalXpress, 2013

Protein clamps tight to telomeres to help prevent aging... and support cancer
Phys.org, 2010

Scientists explore the structure of a key region of longevity protein telomerase
Phys.org

Lab identifies elusive telomere RNA subunit in single cell model
Phys.org, 2007

Dr. Jekyll & Mr. Hyde: Telomere and telomerase in stem cells
Phys.org, 2015

Powered by: TREND MD

Most Popular *this week*

HEALTH & MEDICINE
- Early-Life Exposure to Dogs May Lessen Risk of Developing Schizophrenia
- Mitochondria Are the 'Canary in the Coal Mine' for Cellular Stress
- Ancient 'Chewing Gum' Yields Insights Into People and Bacteria of the Past

MIND & BRAIN
- Researchers Reconstruct Spoken Words as Processed in Nonhuman Primate Brains
- Researchers Discover Brain Circuit Linked to Food Impulsivity
- Changes in the Immune System Explain Why Belly Fat Is Bad for Thinking

LIVING & WELL
- Boy or Girl? It's in the Father's Genes
- Blue Light May Not Be as Disruptive to Our Sleep Patterns as Originally Thought
- Me, Me, Me! How Narcissism Changes Throughout Life

Strange & Offbeat

HEALTH & MEDICINE
- Ancient 'Chewing Gum' Yields Insights Into People and Bacteria of the Past
- New CRISPR-Based System Targets Amplified Antibiotic-Resistant Genes
- Synthetic Nanopores Made from DNA

MIND & BRAIN
- Dogs Process Numerical Quantities in Similar Brain Region as Humans
- Researchers Reconstruct Spoken Words as Processed in Nonhuman Primate Brains
- How Playing the Drums Changes the Brain

LIVING & WELL
- Through the Eyes of Animals
- Babies in the Womb May See More Than We Thought
- Some Hyper-Realistic Masks More Believable Than Human Faces, Study Suggests