Elizabeth Blackburn, Carol Greider and Jack Szostak's Telomere and Telomerase Experiments (1982-1989) [1]

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Experiments conducted by Elizabeth Blackburn, Carol Greider, and Jack Szostak from 1982 to 1989 provided theories of how the ends of chromosomes, called telomeres, and the enzyme that repairs telomeres, called telomerase, worked. The experiments took place at the Sidney Farber Cancer Institute and at Harvard Medical School in Boston, Massachusetts, and at the University of California in Berkeley, California. For their research on telomeres and telomerase, Blackburn, Greider, and Szostak received the Nobel Prize in Physiology or Medicine [3] in 2009. Telomeres and telomerase affect the lifespan of mammalian cells and ensure that cells rapidly develop within developing embryos.

The scientists involved in the experiments with telomeres and telomerase came from a variety of disciplines. Blackburn worked at the University of California in Berkeley (UC Berkeley) from 1982 to 1989. In 1975, she had received her PhD in molecular and cellular biology from the University of Cambridge in Cambridge, England, after which she did postdoctoral work with Joseph Gall at Yale University [4] in New Haven, Connecticut from 1975 to 1977.

As Blackburn's graduate student, Greider studied telomeres and telomerase at UC Berkeley from 1984 to 1987. Greider received her PhD in molecular biology in 1987 from UC Berkeley and continued her research with Blackburn through 1989. Szostak had received his PhD in biochemistry from Cornell University [5] in Ithaca, New York, in 1977, where he specialized in cloning yeast and in manipulating genes [7]. Szostak began to study telomeres and telomerase after hearing a conference presentation given by Blackburn in 1980, during which she explained her work on telomeres in Tetrahymena [9], a single-celled freshwater organism. After meeting Blackburn and discussing her work, Szostak accepted a position at Harvard Medical School [2] in 1982, where he and Blackburn collaborated to investigate the functions of the telomeres of Tetrahymena in yeast.

Blackburn and Szostak's 1982 experiment addressed an issue with how DNA replicates copies of itself within a cell. The issue was that after replication, one of the two DNA strands remains incomplete. When a cell replicates itself, the end of a strand of chromosomal DNA, the telomere [9], shortens. The telomere [9] shortens because the enzyme that replicates DNA, DNA polymerase, only works in one direction on DNA. This process creates what scientists call a leading and a lagging strand during DNA duplication. The leading strand is named such because DNA polymerase moves in one direction across the nucleotide sequence, and replicates the DNA without any breaks in the genetic material. The lagging strand is composed of individual fragments of DNA formed by DNA polymerase (Okazaki fragments) that are later sealed together by the enzyme DNA ligase to create one continuous strand. This strand is called the lagging strand because it can take longer to seal together the individual DNA fragments than the leading strand takes to continuously replicate a strand. The DNA polymerase detaches at the end of the lagging strand and leaves a space that measures a few nucleotides in length. The identity of those nucleotides remained unknown until Szostak and Blackburn published their results in 1982.

To identify the nucleotides, Szostak and Blackburn removed what Blackburn hypothesized were the telomeres in Tetrahymena. The hypothesized telomeres were highly repetitive nucleotide segments of DNA at the ends of chromosomes. The researchers placed the telomeres in circular genetic material, called linearized plasmids, from yeast species. Blackburn and Szostak used yeast and Tetrahymena because of their distant evolutionary relationship from each other, and to see if the telomeres were similar across different species of eukaryotes. They found that the yeast added new DNA to the Tetrahymena telomeres, which led the researchers to conclude that telomeres were highly conserved evolutionarily, or similar across distantly related species, across yeast and Tetrahymena, and hypothetically across other species. Additionally, Blackburn and Szostak observed that the telomeres functioned similarly to each other in yeast and Tetrahymena. Blackburn and Szostak cut out pieces of the similar telomeres from each species and identified them by describing their sequences of nucleotides (DNA sequencing). The experiment confirmed the description of the telomere [9] as a highly repetitive nucleotide segment, particularly rich in the nucleotide guanine, which accumulates at one end of chromosomal DNA.

In 1985, Greider and Blackburn further investigated the mechanism by which DNA was added to the ends of telomeres. Blackburn and Greider noted the composition of telomere [9] ends, but they could not explain what was adding the guanine-rich ends to the DNA. In different species, the lengths of telomeres differ, and with the sequencing techniques available in the 1980s, scientists couldn't determine how DNA was added to the ends of telomeres. Telomeres also appeared to grow over time in
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Subject

Topic
Experiments [29]

Publisher
Arizona State University. School of Life Sciences. Center for Biology and Society. Embryo Project Encyclopedia.

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Format
Articles [30]

Last Modified
Wednesday, July 4, 2018 - 04:40

DC Date Accessioned
Tuesday, March 24, 2015 - 22:59

DC Date Available
Tuesday, March 24, 2015 - 22:59

DC Date Created
2015-03-24

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