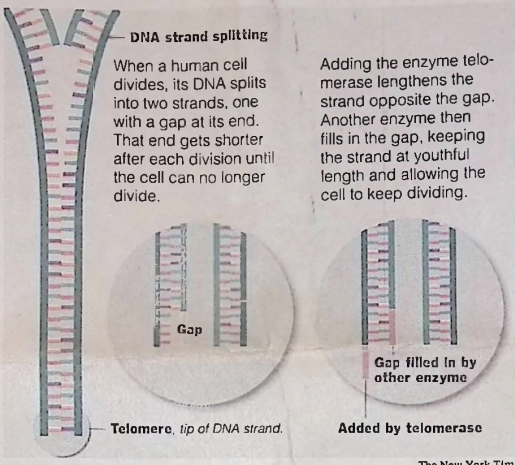
issue an appropriate condemnation.

NYT 1/14/98

Cells' Life Stretched in Lab



The New York Times

Hope on Aging but Concern About Cancer

By NICHOLAS WADE

In a finding that suggests the thread of life can be extended, at least for human cells, biologists have succeeded for the first time in coaxing cells grown in a test tube to live far beyond the limit at which they usually fail.

The finding may help answer the question of why human cells age, and may also offer a practical means of treating certain diseases by rejuvenating aging cells.

Despite some scientists' euphoric talk about the discovery of a cellular "fountain of youth," others cautioned that the cell senescence mechanism is also a principal defense against cancer, and that bypassing it could be dangerous.

The finding makes use of a newly discovered human gene that resets an inherent limit imposed by nature on the number of times a human cell can divide. Human cells grown in a test tube will usually divide about 50 times. But cells that have undergone the new treatment have bypassed this limit and as of today have divided 90 times with no sign of abnormality.

The result has broad scientific and medical interest because it elucidates a mechanism in living cells that is central both to aging and to cancer. Although the mechanism, known as telomere shortening, has long been suspected to work this way, proof has been unattainable until now.

The Geron Corporation of Menlo Park, Calif., which owns or has applied for several patents on the gene, known as the telomerase gene, says its technology will rejuvenate cells involved in age-related diseases and help diagnose and treat cancer.

"These cells have an indefinite life span as far as you can tell," said Dr. Calvin B. Harley, an author of the new finding and vice president of Geron.

Another author of the study, Dr. Jerry W. Shay, said the finding would "now allow us to take a person's own cells, manipulate

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Associated Press

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great Speaker."

Human Cells' Life Stretched, Opening New Vista on Aging

Continued From Page A1

and rejuvenate them and give them back to the same patient." The rejuvenated cells could help grow new skin for burn victims and aid people with diseases caused by the failure of aging cells to divide, like macular degeneration, said Dr. Shay of the University of Texas Southwestern Medical Center.

The new research was conducted by two teams of scientists led by Dr. Harley at Geron and by Dr. Shay and Dr. Woodring E. Wright of the Texas medical center. Their work is reported in this week's issue of the journal Science.

Disclosure of the findings yesterday sent Geron's stock up 44 percent on the Nasdaq stock exchange, where it closed at $14.375 a share.

Experts cautioned that as important as the new results were, there was a Catch-22 in the way evolution had designed the telomerase system. The mechanism almost certainly evolved, at least in humans, as a way to limit cancer. Hence any medical use of rejuvenated cells in which the division limit has been subverted may weaken one of the body's salient defenses against tumors.

"Geron would have us believe that telomerase is the key to immortal life, and I have no idea if there is any wisp of truth in that," said Dr. Robert Weinberg, a leading expert on cancer genetics at the Whitehead Institute in Boston.

The mechanism at the heart of the new work is a system developed by certain living cells for managing their chromosomes, the rod-shaped structures in which the cell packages its genetic programming tapes. The device that copies the long double helix of DNA when the cell divides has a peculiar defect: it cannot copy the last few units of DNA at the chromosome's tip. So each time a cell divides, its chromosomes get a little shorter. The end section of the chromosomes, known as the telomere, thus resembles some thread of life that is used as the tally for counting off cell divisions. When it runs out, that means that the cell's ability to divide is gone.

This tempting analogy became much strengthened when biologists found that all human cells possess a gene whose product, named telomerase, can lengthen the telomeres. In normal cells, the gene is firmly silenced. But in human germ line cells, the egg and sperm, telomerase is active and maintains the telomeres at a constant length — some 15,000 chemical letters of DNA. It is also active in cancer cells, which have learned to switch on telomerase and bypass a mechanism that would otherwise shut them down.

Skeptics of this theory began to question whether the telomerase shortening was really as important as advertised. Last year Dr. Carol W. Greider of Johns Hopkins University engineered a breed of mice that lacked a telomerase gene. The mice are alive and well after several generations, and their cells show no particular cancerous tendencies.

Talk of a cellular 'fountain of youth' is a bit premature.

"The theory came under tremendous skepticism," said Dr. Harley, who was one of its earliest proponents. "People said it was gibberish or based on theology."

The discovery last year of the human telomerase gene has at last allowed Dr. Harley to put the theory to rigorous test. Inserting this gene into human cells, along with a signal that forced the gene to become active, he and his colleagues found that the cells quickly built their telomeres back up to youthful length, and continued to divide long past the usual limit.

"Our results indicate that telomere loss in the absence of telomerase is the intrinsic timing mechanism that controls the number of cell divisions prior to senescence," the biologists write in their report.

Dr. Leonard Guarente, an expert on cellular aging at M.I.T., described the research as "a beautiful piece of work" but said its relation to human aging remained to be defined.

Dr. Weinberg of the Whitehead Institute, a cancer expert who has recently entered the telomere field, said the finding was relevant to the senescence of human cells, but not necessarily to that of the human body. "If it were true that our life span is dictated by telomere shortening, then you would imagine that some humans die because their critical cells run out of telomeres, but there is no evidence for that at all. The Geron people are pushing this hard, but to my mind there is not much evidence for it."

Dr. Weinberg suggested that everyone might have enough telomeres to live to be 200. What limits human life span is disease, especially cancer, and the telomere shortening system is a way of insuring that the growth of incipient cancer cells is quickly halted.

"If you put telomerase into all ou cells maybe they could live longer, Dr. Weinberg said, "but on balance would be a very bad thing because would no longer prevent those cel from growing without limits, and the end malignancy is the greate threat to human longevity."

dy Shows Smoke Is Linked Faster Hardening of Arteries

AGO, Jan. 13 (AP) — Ciga-
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dy suggests.
authors, led by Dr. George
d, an epidemiologist at Wake
University in Winston-Salem,
stimated that 30,000 to 60,000
a year in the United States
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The study is being published
nesday in The Journal of the
an Medical Association.
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hand smoke, like active smok-
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versible problems, like thick-
of the blood.
American Heart Association,
advocates banning smoking in
blic places, said the study was
rst to link secondhand smoke
narrowing in the carotid arteries, which carry blood to the brain. That narrowing "indicates that other blood vessels are similarly affected, including ones in the heart muscle," the association said.

Dr. Stanton A. Glantz of the University of California at San Francisco, an expert on secondhand smoke, said the study provided "a real important bridge" between studies that have found that cigarette smoke causes deteriorating arteries and studies showing that passive smokers have an increased risk of fatal heart attacks.

"This fills in that missing link," Dr. Glantz said.

Tom Lauria, a spokesman for the Tobacco Institute, which is financed by the tobacco industry, said it had not yet evaluated the study. But Mr. Lauria noted: "The majority of studies do not show any increased risk for nonsmokers. We consider the science to be inconclusive."