A spate of recent mind–body research studies that could prove important to cancer patients suggest that counseling and exercise can undo some of the changes wrought by stress at the cellular level.

Scientists have known for two decades that telomeres—stretches of DNA that protect the ends of chromosomes and, thus, the integrity of the genome—shorten with aging. More recently, evidence has mounted that shorter telomeres are associated with shorter lives and with an array of diseases, including cardiovascular disease and several cancers. Studies have also associated smoking, high body mass index, depression, and physical inactivity with diminished telomere length.

In 2004, Elizabeth Blackburn, Ph.D., the University of California, San Francisco, biochemist who won the Nobel Prize for her work with telomeres, and her colleagues first demonstrated, in
Studies on Stress and Telomeres

At the April 2011 meeting of the American Association for Cancer Research (AACR) in Orlando, Nelson presented results of a small prospective study of cervical cancer survivors who had been randomized to receive either usual care or usual care plus six psycho-social telephone counseling sessions designed by Nelson’s coinvestigator, Lari Wenzel, Ph.D. In the original study, published in 2008, the counseling intervention improved patients’ quality of life and modulated stress-associated biomarkers such as cortisol, DHEA, and immunological status. For the new study, they tested archived blood specimens from those patients and discovered that improvement in the stress response was associated with increased telomere length.

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Other Factors in Telomere Length

The UCSF group found that perceived stress was related not only to telomere length but also to high levels of interleukin 1b, a pro-inflammatory cytokine. Steven Cole, Ph.D., a genomics researcher and associate professor of hematology and oncology at UCLA’s Jonsson Comprehensive Cancer Center, said that finding was consistent with those of other studies.

Cole and his colleagues published a paper in the Sept. 15, 2010, issue of Cancer Research, showing that chronic stress fueled breast cancer metastasis in a mouse model by producing inflammation. Animals that had been stressed by being confined in a small area had a 30-fold increase in cancer spread to distant tissues, including the lungs and lymph nodes, compared with unstressed animals. Stress signaling from the sympathetic nervous system enhanced the recruitment of macrophages to the primary tumor site, which turned on inflammation genes. The immune response modified the tumor microenvironment and extracellular matrix, allowing cancer cells to escape from the tumor. However, treating the stressed animals with the beta blocker propranolol reversed the stress-induced macrophage infiltration and inhibited the metastases.

“It looks like one of the major dynamics affecting telomere length is also implicated in breast cancer metastasis,” said Cole. “In both cases, the driver is inflammation, which causes cells to change their behavior. In our breast cancer model, the tumor cell is being influenced by the macrophages to...
dissolve the extracellular matrix. In telomeres, inflammation can cause immune cells to proliferate, which causes their telomeres to shorten.”

Taking their mouse research into human subjects, Cole and Patricia Ganz, M.D., director of cancer prevention research at the Jonsson center, looked at data from a California cancer registry of women with early-stage breast cancer. They reported in the April 11, 2011, issue of Breast Cancer Research and Treatment that women who took beta blockers to control hypertension had a statistically significantly lower risk of breast cancer recurrence than those who took ACE (angiotensin-converting enzyme) inhibitors. Cole said those observations, though consistent with the preclinical data, need to be confirmed in randomized trials.

**Genes Behind Telomere Length**

Although inflammation appears to play a role in mediating the physiologic effects of stress, including telomere shortening, it is only part of the story. A genetic factor is probably also at work. In another study presented at AACR, researchers from the University of Texas M. D. Anderson Cancer Center in Houston reported that a common genetic variation was linked to both bladder cancer risk and telomere length.

Jian Gu, Ph.D., assistant professor of epidemiology at M. D. Anderson, said a single-nucleotide polymorphism (SNP) on chromosome 14 was associated with reduced risk of bladder cancer and increased telomere length. Previous studies had tied telomere length to either cancer risk or genetic variation, but Gu’s report was the first to make both connections, according to Blackburn, who appeared at a press conference with Gu and Nelson to discuss their findings. Gu’s article and an editorial by Blackburn also appear in the April issue of Cancer Prevention Research.

Blackburn noted that in Gu’s study, both the SNP and smoking affected the risk of bladder cancer, with smoking exerting the larger effect. “The broader question of great interest,” she wrote in the editorial, “is whether nonalterable genomic factors (SNPs such as those reported by Gu and colleagues) synergize with potentially malleable nongenetic influences (e.g., lifestyle, behavioral, stress, and environmental factors).” Blackburn is among the founders of Telome Health, a private telomere testing service.

“Telomere length represents an integrated marker of your lifelong exposures to both positive and negative factors,” said Calvin Harley, Ph.D., president and chief scientific officer of Telome Health. “It’s not organ specific, like cholesterol, but a global marker for disease risk and overall health. More importantly, telomere length can be modified by lifestyle changes: You’re not stuck with what you’re born with.” However, telomere length testing is still in the “research and development phase in terms of how to use it in an oncology setting,” he emphasized.

Telomere science has attracted the attention of supplement and pharmaceutical manufacturers, too. New York–based T.A. Sciences is already marketing a nutraceutical that the company claims activates telomerase, the enzyme that replenishes telomeres. Meanwhile, Sierra Sciences of Reno, Nev., is developing a drug that its founder, Bill Andrews, Ph.D., believes will reverse aging. Andrews said that product is still years off, but in his opinion a recent paper by Ronald DePinho, M.D., of the Dana–Farber Cancer Institute in Boston, offered proof of principle. That paper, in the Jan. 6, 2011, issue of Nature, reported that DePinho and colleagues had reversed the aging process in telomerase-deficient mice, increasing the size of their shrunken brains and restoring their diminished olfactory sense. Meanwhile, Andrews said, his company is involved in the “prelaunch of a natural product” that supports telomeres.

**Telomere Research and Oncology**

Some researchers worry that these interpretations are premature, especially for oncology. “There are consistent data for the association of telomere length with cardiovascular disease and cardiovascular disease–related death,” said Yun-Ling Zheng, M.D., Ph.D., a molecular epidemiologist at Georgetown University. “As for the association of telomere length and cancer risk, however, the data are not as consistent.”

Zheng’s concern stems from the fact that telomerase is a “multifunctional enzyme.” Although the enzyme maintains telomere length, it also plays a role in cell-proliferation signaling. “Increased telomerase activity may have an antiaging function,” she said, “but 80%–90% of solid tumors have high telomerase activity. If we rush into producing drugs and supplements that activate telomerase, the public should be aware of the potential side effects, such as increased cancer risk.”

Cole added, “Many of us are still not sure how much information telomere length really conveys about your likelihood of becoming ill or dead. We’re generally measuring telomere length in blood cells, which may not tell you much about telomere length in your brain cells, muscles cells, heart cells, and other tissues. But if telomere length functions as a really good measure of the accumulated influence of inflammation and other forms of wear and tear on cells throughout your body, then it may well prove valuable. Right now, I think most people agree that we need more research to understand how best to interpret this really fascinating measure of cellular aging in terms of aging of the total human body.”