diabetes, hyperlipidaemia, or obesity,[12] whether large, comprehensive randomised trials addressing the use of such interventions in obese patients with prostate cancer are even needed could be questioned. Most men with prostate cancer die of causes other than prostate cancer, and therefore oncologists should already be recommending lifestyle changes to all patients, especially to those who are overweight or diabetic. A message from oncologists advocating healthier lifestyles might improve our patients' cardiovascular and metabolic clinical profiles, but might also modify the tumour-cell medium for an improved patient outcome.

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Telomerase and the benefits of healthy living

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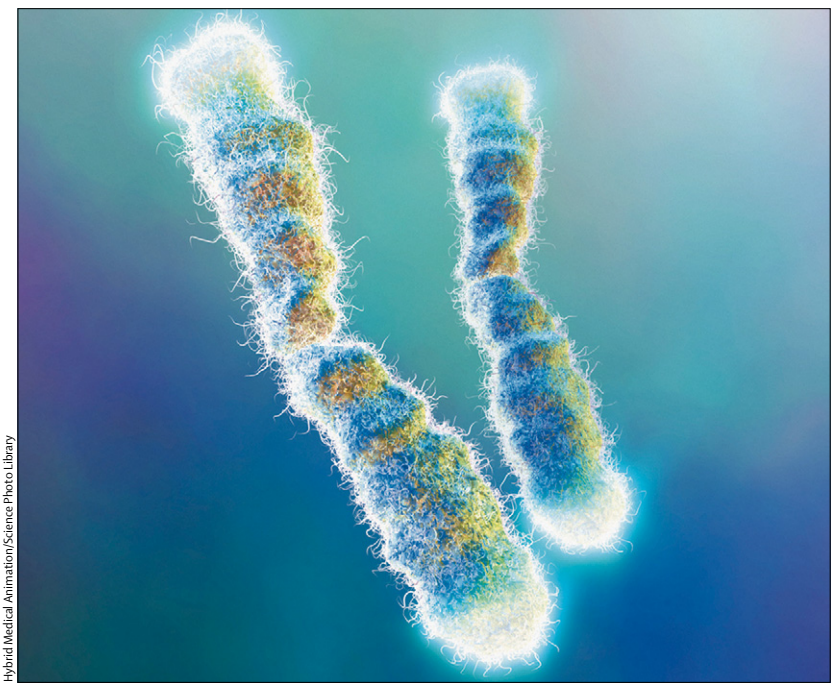
Telomeres are important cellular structures whose integrity is essential for maintaining cell viability. There is now clear evidence that links telomeres and their associated proteins to cancer, cardiovascular disease, and ageing. Therefore, understanding the function of this biological system is attracting much attention, in an effort to use the information as a means to combat cancer and age-related diseases.

Telomeres prevent the loss of essential genetic information by overcoming the "end replication problem" that arises from the inability of the cell's replication machinery to synthesise the ends of linear chromosomes. Telomeres recruit shelterin, a multiprotein complex that helps form a loop on the ends of the chromosomes. This structure prevents the ends from being recognised as DNA strand breaks by the cell's recombination and DNA-repair systems, which would lead to chromosome end-to-end fusion, genomic instability and senescence.[1,2] The telomere's capacity to provide genomic stability is diminished over time as a result of a natural loss of telomeric structure and the reduced ability of the enzyme telomerase to synthesise telomeric repeats.[3,4]

Leonard Hayflick identified the importance of telomeres in maintaining cellular viability in 1961. He noted that cultured human and mammalian cells stopped dividing after roughly 50 cell divisions, which prevented the telomeres from subsequently becoming too short to protect the genome.[5] As a self-preservation mechanism, in order to avoid genomic instability and protect the organism from catastrophic diseases, such as cancer and cardiovascular disease, cells shut themselves down by entering a state of replicative senescence–the hallmark of ageing.

Telomere shortening leads to cellular ageing, a process that can theoretically be reversed by restoration of telomeric structures. Telomerase, the enzyme that replicates telomeres, is therefore an ideal target for the identification and development of activators that could facilitate cell proliferation and tissue renewal. Telomerase is a DNA polymerase that consists of a protein, Telomerase Reverse Transcriptase (TERT), and an RNA component, Telomerase RNA (TER), which TERT uses as a template for the addition of short, G-rich repeats at the ends of chromosomes.[6,7] One possibility to counteract the loss of telomeric structure and cell ageing



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Telomeres help prevent the loss of genetic information

might be stimulation of telomerase activity through administration of an enzyme activator, although no such compounds have been identified.

In a landmark study, in this month's issue of *The Lancet Oncology*, Ornish and co-workers[8] report a key finding in the search for ways to activate telomerase. They showed that adopting a healthy lifestyle in a group of thirty patients aged 49 to 80 years increased the concentrations of telomerase in peripheral-blood mononuclear cells (PBMCs), an important result because the enzyme is not usually expressed in adult somatic cells. Specifically, the group noted that a healthy diet, exercise, and stress management led to reductions in psychological distress and low-density lipoprotein cholesterol, resulting in a significant (30%) increase in telomerase activity in the patients' PBMCs. Several studies have shown that overproduction of psychological stress-related hormones, such as catecholamines and cortisol, causes oxidative cell damage, which can compromise telomere maintenance and replication systems.[9] Increasing the cell's concentration of telomerase, such as by exercise and diet as Blackburn's study found, is thought to lengthen the telomeres, thereby providing the chromosomal stability that is associated with tissue renewal and disease prevention.

Identifying activators of telomerase that could complement the benefits of a healthy lifestyle will be an important focus in ongoing investigations of the telomeric system. Understanding the precise mechanism of telomerase upregulation seen in PBMCs on a healthy diet and exercise regime might facilitate efforts to produce such activator compounds. However, telomerase is highly active in almost 90% of human cancers and absent in adjacent healthy tissues.[9,10] We should therefore investigate the pathways and mechanisms by which the telomeric complex balances cell proliferation and tissue renewal with the risk of tumour formation.

Although the advantages are clearly holistic, adopting a healthy lifestyle is not always possible in today's world, where stress and a fast food diet are the norm. At the cellular level, the benefits of a healthy diet and regular exercise have been studied extensively, and attributed to the production of compounds that counteract the effect of free radical products of oxidative stress that can cause substantial damage to our DNA. This new finding that a healthy diet and exercise can also upregulate telomerase concentrations in non-carcinogenic cells is an exciting outcome, and should encourage people to adopt a healthy lifestyle in order to avoid or combat cancer and age-related diseases.

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