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Is telomerase the cure-all and end-all? ▼

Detection of the enzyme telomerase has been touted as a marker for cancer diagnostics, as the next molecular target for cancer therapy and as an agent for cell regeneration, tissue engineering and perhaps mammalian cloning. Pretty amazing when one considers that its only known function is telomere maintenance in cells of the germline, stem cells and immortal and/or cancer cells. Can one molecule really make that much of a difference?

In 1985, through the ingenuity of Greider and Blackburn, telomerase was discovered and the field was born [1]. Not until 1994 was it observed that human cancers, but not normal somatic tissue, had telomerase activity [2]. Development of a highly sensitive, clinically friendly assay [3] caused telomerase to explode onto the scene, with the publication of hundreds of articles on telomerase expression in cancer. Because of its association with nearly 90% of all human cancers, telomerase has become a likely diagnostic tool. Is it possible that, because telomerase is expressed in the vast majority of human tumors, its detection would replace traditional pathology? It seems doubtful but telomerase assessment could be useful for the diagnosis of borderline cases or for the early detection of progressive disease.

As a target for cancer therapeutics, targeting telomerase could be useful, but it will most certainly not be the initial treatment. Blocking telomerase function typically results in delayed cellular effects (senescence or apoptosis), where cells will divide normally for 10–100 days, shorten telomeres and eventually arrest or die. If one were to treat a primary tumor with telomerase inhibitory compounds as a primary defense, the tumor would continue to grow until senescence or apoptosis is achieved and would probably become so large as to cause additional health problems. In fact, anti-telomerase therapy might only be useful after the primary tumor has been excised, where inhibition of telomerase would negatively affect the growth potential of any tumor cells that remain. However, if telomerase is inhibited, the alternative telomere maintenance pathway [4] could be activated, although, to date, this phenomenon has not been observed following telomerase inhibition.

One additional milestone in the telomerase saga concerns proof of the Telomere Hypothesis (stated as 'progressive telomere shortening in normal cells results in cellular senescence'), which was observed in 1998 when telomerase was expressed in primary cells and senescence was abolished [5]. Allowing normal cells to proliferate continuously without the changes that are typically associated with progression to cancer provides a tremendous number of possible uses, including, but not limited to, tissue regeneration and mammalian cloning. With respect to regeneration [6], the introduction of human telomerase in bovine adrenocortical cells provides increased growth potential *in vitro*, and when transplanted into mice without adrenal glands, functional tissue regeneration occurs, whereas similarly aged cells without telomerase were unable to regenerate.

Clearly, telomerase has multiple uses, which is quite amazing considering that it only has a single defined function. Telomerase appears to be the next 'Great Hope' in a long line of hopeful targets, but only time will tell as to how useful telomerase will be in terms of cancer therapeutics, tissue regeneration and, potentially, human cloning.

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Shawn E. Holt
Assistant Professor
Medical College of Virginia at Virginia Commonwealth University
Richmond, VA, USA

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