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# Telomerase in Cancer: Diagnostic, Prognostic and Therapeutic Implications

# Telomerase in Cancer: Diagnostic, Prognostic, and Therapeutic Implications

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Maintenance of telomere stability is required for cells to escape from replicative senescence and proliferate indefinitely. Telomerase is upregulated/reactivated in nearly all human cancers.[1] Telomerase catalyzes the synthesis and extension of telomeric TTAGGG repeats stabilizing telomere length. The correlation between telomerase activity and human tumors suggests that tumor growth almost universally requires reactivation of telomerase. There is experimental evidence from hundreds of independent laboratories that telomerase activity is present in nearly all human tumors but not in normal tissues. Thus, clinical telomerase research is focused on the development of methods for accurate diagnosis of cancer and on novel anti-telomerase cancer therapeutics.[2]

There has been a vast increase in telomerase research over the past several years, with many different pre-clinical approaches being tested for inhibiting telomerase activity as a novel therapeutic modality to treat malignancy.[3] To confirm action through a telomerase-dependent mechanism, inhibitors but not chemically-related molecules should reduce telomerase activity but not initially affect cell growth rates; should lead to progressive shortening of telomeres with each cell division; and ultimately cause cells to undergo growth arrest/apoptosis in a time-frame dependent on initial telomere length. This approach has been validated using antisense oligonucleotides directed against the telomerase RNA template region,[4] expression of a dominant-negative version of the catalytic protein component (hTERT) to competitively inhibit endogenous telomerase from maintaining telomeres,[5] and by using a small molecule inhibitor of telomerase.[6] Other approaches not requiring a time delay for efficacy include the use of telomerase promoter/suicide pro-apoptotic gene therapy or use of immunotherapy directed against telomerase-specific peptides.[3-7] In these approaches, only telomerase-expressing cells should be killed. In some instances, telomerase inhibitors would be used in an adjuvant setting in combination with standard treatments, as well as in combination with new agents such as gene therapy and angiogenesis inhibitors.[3] Telomerase inhibitors could also be used to prevent cancer in susceptible populations or following standard therapies in which there is no clinical evidence of disease to treat possible micrometastases and thus prevent cancer relapse.[5]

For additional information see review issue of the journal Oncogene (Volume 21, Number 4, January 21, *2002)* on Telomeres and Telomerase.

## References


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