

## Telomerase Biology in Animal Cancers

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Cancer is a terrifying word in the mind of human beings. Over the past three decades, tremendous progress has been made in our understanding of cancer. The development of molecular biology has given researchers more motivation to understand the nuanced and intricate molecular processes involved in carcinogenesis, opening up the possibility of creating novel diagnostic and treatment approaches. By devoted study and the persistent efforts of oncologists around the world, many of the complexities of this particular disease are still being ironed out.

Telomeres are specialized nucleoprotein structures at the ends of eukaryotic chromosomes that are crucial for stable chromosome maintenance. These telomeres comprised up of multiple kilobases of repeating, simple sequences (TTAGGG), as well as accompanying proteins that attach to these repeating sequences. The repeat sequences of telomeres are conserved among the species. Telomeres capping the chromosome termini are essential to avoid abnormal recombination and end-to-end fusions, safeguard chromosomes against exonucleolytic (DNA) degradation, and preserve nuclear integrity. Telomeres may also play a role in the control of genes at distant loci.

It has been demonstrated that telomeres shorten with each cell division *in vitro* and with increasing age *in vivo*. Telomere shortening might serve as a mitotic clock that counts the number of divisions a cell can undergo. This telomere shortening is thought to be caused by a lack of activity of an enzyme called telomerase. This telomerase activity is frequently detected in cancer cells from a wide range of human and animal tumors. Cancer cells, on the other hand, have shorter but more stable telomeres than normal cells. This suggests that telomeres have been gradually shortening with each cancer cell division until a certain point, at which point either some mechanism led to the commencement of their maintenance or the cells died. In the latter case, cancer cells would experience

terminal growth arrest, tumor stasis, and regression called cellular senescence.

Telomerase has emerged as a near universal marker of malignancy and has thus become an obvious diagnostic and therapeutic target because it is commonly expressed in a wide variety of cancers. The frequent presence of telomerase activity in a range of normal cells and tissues may put a cap on the use of telomerase as a cancer diagnostic. The majority of normal mammalian brain cells are post-mitotic, and there is no telomerase expression. As a result, telomerase activity in brain tumors is a useful diagnostic sign. However, the brain tissue appears to be unique in this regard. Fortunately, it is also discovered that benign neoplastic tumors lack telomerase activity. Although the extent to which telomerase expression is particular to the malignant state and the period of cancer growth during which it is activated is critical, for using telomerase as a diagnostic tool. The presence of telomerase in epithelial stem cells has produced conflicting outcomes in conditions such colonic adenomas, esophageal, cervix, and pre-menopausal endometrium, cervix, colon, and tissues harboring activated lymphocytes.

Detection techniques for telomerase and telomere:

<b>Telomerase and telomere</b>	<b>Detection techniques</b>
Telomerase activity	TRAP assay
Telomerase gene expression	Northern blot Nuclease protection assay RT-PCR In situ hybridization immunohistochemistry
Telomere length	Southern blot In situ hybridization Flow cytometry
Senescence-like phenotype	SA b-galactosidase activity P16 expression P21 expression

In veterinary oncology, the use of telomerase activity assays such the TRAP (telomere repeat amplification protocol) and TRAP-ELIDA assays is still in its infancy. Even the confirmatory study showing the presence of TTAGGG repeat sequences in bovine embryo chromosomes and telomerase activity in embryonic developing stage was published in 1999, which is astonishing. The research on the use of telomerase as a diagnostic marker for animal neoplasms, however, just began to appear in 1996. The majority of telomerase research in animals are carried out in canine cancers using the TRAP assay. It is noteworthy that this marker demonstrated significantly higher sensitivity (88% - 95%) in animal tumors than in human tumors. A study reported that telomerase activity was shown to be less



specific (83%) than cytological examination (100%). Considering the piece-meal but promising reports, one should be optimistic that telomerase as a diagnostic marker in veterinary oncology holds promise for the future.

**Telomerase activity in animal cancer diagnosis:**

<b>Tumors</b>	<b>Species</b>
Malignant melanomers	Dog, pig, horse, opossum and man
Canine venereal tumours, canine mammary tumors, canine perianal tumors, equine wart, bovine bladder cancer	Dog, cattle and horse
Malignant and benign tumors	Dog
Mammary tumors, skin and oral cavity tumors, vascular tumors, Sertoli cell tumors	Dog
Benign and malignant mixed tumors, adenocarcinoma	Dog

