Telomerase in canine cancers: a potential model system for human cancer studies

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Normal cells, at least *in vitro*, have a defined lifespan, replicating for a limited number of divisions after which they undergoe an irreversible growth arrest termed replicative or cellular senescence. The mechanisms of cellular senescence have been extensively investigated in human cells and are atleast in part controlled by telomeres, the extreme ends of linear chromosomes. With increasing cell division, telomeres undergo continual attrition which ultimately acts as a trigger for the cell to exit the cell cycle. In contrast, cancer cells and immortalised cells can proliferate indefinitely and can bypass the growth arrest constraints that ensue with increased cell divisions, by reactivation of the enzyme telomerase. To elucidate the role of telomerase in canine neoplasia, we have evaluated telomerase activity in a wide range of canine tissues and primary cultured fibroblasts and immortalised cultures. These studies have shown telomerase is associated with immortalisation and is absent from most normal canine tissues, with the exception of cells with a high proliferative potential. The tumour specificity of telomerase has led us to investigate telomerase based targeting approaches for treatment of canine cancers *in vitro*. More specifically, we have evaluated telomerase inhibition *in vitro* using dominant negative mutants of the catalytic reverse transcriptase and reverse transcriptase inhibitors. Further we have investigated gene targeting in telomerase positive and negative cells lines using human telomerase promoter elements. Our studies in the dog have identified telomerase as a target for therapy and our increasing understanding of the biology of telomerase in the dogs may lead to the development of novel therapeutic approaches for cancer therapy. Further, our data supports the dog as a potential model system for human cancer studies.