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Samarakkody S.W.M.A, Ranathunga R.M.S.T REGULATION OF TELOMERASE IN TUMORIGENESIS Tutor: Grigorovich V.V.

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Telomerase, a ribonucleoprotein enzyme complex and cellular reverse transcriptase. Telomeres need telomerase activity to preserve their total length which protects these chromosomal end regions known as telomeres. The genetic stability related to this process enables proper cell function. The current knowledge gap focuses on *TERT* promoter mutations. The up-regulation of telomerase occurs due to the *TERT* promoter mutations which leads to cell immortalization in newly developed cancer cells. Multiple factors delay the advancement of targeted therapies because of unclear tumorigenic mechanisms that originate from the existing gap.

This study focuses on tracking how telomerase controls tumor development because such knowledge will help doctors develop treatment strategies for medicine.

The research study utilized data from AACR Project GENIE 11.0 registry to evaluate *TERT* promoter mutations across ten different solid tumor types according to articles present in PubMed and PNAS.

TERT promoter mutations determined tumor aggressiveness rates of 83.9% in glioblastoma and 44.2% in hepatocellular carcinoma and 66.6% in urothelial carcinoma. The cellular mutations elevated TERT mRNA transcripts and telomerase activity together with increasing telomere length through blocking the silencing mechanism. The expression of elevated TERT mRNA presents in an opposite trend with the opposite pattern. Post-transcriptional regulation appears to exist because reasonable telomerase activation occurs together with elevated TERT mRNA expression.

The variation of *TERT* promoter mutations between tumors presents possible treatment opportunities. Tumors of glioblastoma display very high occurrence rates of *TERT* promoter mutations at 83.9% while urothelial carcinoma shows significantly lower rates at 44.2%. The data implies that particular tumors established robust chemoresistant platforms while operating under telomerase activation standards for commercial guidance.

TERT promoter mutations drive the activation of telomerase resulting in tumor development according to research evidence. Studies show diverse ways to maintain telomeres yet emphasize altering telomerase as a crucial upcoming therapeutic strategy. Progressive research needs to study post-transcriptional regulatory systems so scientists can develop more specific cancer treatments.