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Expression of telomerase reverse transcriptase in soft tissue tumor in conjunction with hypoxia-inducible factor-1 α , tumor angiogenesis and related molecules P53, P21, Rb, Ki67 and Mdm2

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Background: Telomerase enzyme is a ribonucleo-protein complex with reverse transcriptase activity. The catalytic subunit (Telomerase reverse transcriptase) TERT correlates with poor clinical outcome in various tumors. Tumors expressing this enzyme may be more aggressive and telomerase activity may be a useful prognostic marker. For soft tissue tumor little is known about telomerase activity and most of reports focus on telomerase activity in liposarcomas.

Aim: This study was conducted to investigate the relationship between expression of the catalytic subunit of telomerase (h-TERT), cell proliferation and hypoxia in a range of soft tissue neoplasms.

Material & methods: A tissue microarray was constructed from 101 cases and whole sections were cut from 21 cases of soft tissue neoplasm. Immunocytochemistry for h-TERT, HIF-1 α , p53, p21, Rb, CD31, Ki67 and MDM2 was done. Western blotting for hTERT protein of 12 sarcomas was performed to validate h-TERT expression.

Results: h-TERT was expressed in 16% of benign and 65% of malignant neoplasms ($p < 0.005$) with higher expression in leiomyosarcomas, synovial sarcomas, undifferentiated sarcomas and myxofibrosarcomas and lower expression in liposarcomas. h-TERT expression was significantly associated with grade ($p = 0.000$), stage ($p = 0.000$) and size of the tumor ($p = 0.02$). Higher expression of HIF-1 α and Ki67, and loss of Rb expression were associated with high grade sarcomas ($p < 0.004$). Expression of p53 and MDM2, p21 and tumor vascularity were not associated with grade. High expression of HIF-1 α and Rb were significantly associated with the stage ($p = 0.002$, 0.03).

Conclusion: hTERT is expressed in a wide range of high grade sarcomas. The positive correlations between proliferation, hypoxia and vascularity support the view that mesenchymal cells are adapted to proliferate in a hypoxic environment. Increased expression of hTERT may be part of this adaptive response.

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