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TRAIL INDUCED APOPTOSIS AND INTERACTION WITH CYTOTOXIC AGENTS IN SOFT TISSUE SARCOMA CELL LINES.

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The sensitivity of four human soft tissue sarcoma (STS) cell lines (HTB-91 [fibrosarcoma], HTB-92 [liposarcoma], HTB-93 [synovial sarcoma] and HTB-94 [chondrosarcoma]) to TNF-related apoptosis-inducing ligand (TRAIL)-mediated apoptosis was investigated. Furthermore, STS cell lines were analyzed for expression levels of TRAIL-receptors R1-R4 as well as of apoptosis-modulating proteins FLICE-like inhibitory protein (FLIP) and osteoprotegerin (OPG).

TRAIL induced significant apoptosis (>90%) in HTB-92 and HTB-93 STS cells, whereas no effect was observed in HTB-91 and HTB-94 STS cells. Expression levels of TRAIL-R1 mRNA were high in TRAIL-sensitive HTB-92 and HTB-93 STS cell lines, as compared to low or undetectable in TRAIL-resistant HTB-91 and HTB-94 STS cell lines. TRAIL-R2, -R3, -R4 mRNA expression did not correlate with TRAIL sensitivity. Furthermore, no correlation of FLIP- or OPG presence with TRAIL resistance was observed in the present model. Co-incubation of TRAIL-resistant HTB-91 and HTB-94 STS cells with doxorubicin plus TRAIL was able to overcome apoptotic resistance to either agent alone. In TRAIL-sensitive HTB-92 and HTB-93 STS cell lines co-incubation of TRAIL with doxorubicin or paclitaxel acted in a synergistic or additive manner, respectively.

Based upon the present data, evaluation of TRAIL application in soft tissue sarcoma in vivo might be considered