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Titel des Beitrags: Is there a role for the Fas-/Fas-Ligand pathway in chemoresistance of human squamous cell carcinomas of the head and neck (SCCHN)?

Abstract: The aim of the present investigation was to determine the expression of the Fas-receptor/ligand system in established cell lines of squamous cell carcinomas of the head and neck (SCCHN), and to study its functional impact on chemotherapy-induced apoptosis in these SCCHN cell lines. We observed constitutive expression of Fas and FasL in 13 SCCHN cell lines by RT-PCR, Southern-blotting and immunocytochemistry, respectively. Administration of the agonistic Fas-antibody CH-11 led to a significant reduction of viable cells in the colorimetric MTT-assay in 5 out of 13 (38%) cell lines tested and preincubation with Interferon-gamma (IFN-gamma) rendered 3 (23%) primarily resistant cell lines sensitive. Cisplatin (cDDP) and bleomycin (BLM) caused dose-dependent cytotoxicity in all cell lines as determined by the 50% inhibitory concentration (IC(50)) and induction of apoptosis. Furthermore, both antineoplastic agents led to an enhanced surface expression of Fas and FasL in all cell lines, and this effect was independent of the respective p53-status. This upregulation of Fas/FasL surface expression increased preexisting Fas-sensitivity only, but failed to make primarily resistant cell lines undergo Fas-mediated growth reduction or apoptosis. Vice versa, blockade of Fas-receptor-ligand-interactions by monoclonal antibodies directed against FasL was able to attenuate
the cytotoxic effect of cDDP and BLM in 2 out of 5 (40%) cell lines tested only. In conclusion, in contrast to many other solid tumors, the Fas/FasL-system does not seem to play an exclusive role in anticancer drug mediated apoptosis in SCCHN.