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Heterogeneous in vitro effects of doxorubicin on gene expression in primary human liposarcoma cultures

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Abstract

Background: Doxorubicin is considered one of the most potent established chemotherapeutics in the treatment of liposarcoma; however, the response rates usually below 30%, are still disappointing. This study was performed to identify gene expression changes in liposarcoma after doxorubicin treatment.

Methods: Cells of 19 primary human liposarcoma were harvested intraoperatively and brought into cell culture. Cells were incubated with doxorubicin for 24 h, RNA was isolated and differential gene expression was analysed by the microarray technique.

Results: A variety of genes involved in apoptosis were up and down regulated in different samples revealing a heterogeneous expression pattern of the 19 primary tumor cell cultures in response to doxorubicin treatment. However, more than 50% of the samples showed up-regulation of pro-apoptotic genes such as *TRAIL Receptor2*, *CDKN1A*, *GADD45A*, *FAS*, *CD40*, *PAWR*, *NFKBIA*, *IER3*, *PSEN1*, *RIPK2*, and *CD44*. The anti-apoptotic genes *TNFAIP3*, *PEA15*, *Bcl2A1*, *NGFB*, and *BIRC3* were also up-regulated. The pro-apoptotic *CD14*, *TIA1*, and *ITGB2* were down-regulated in more than 50% of the tumor cultures after treatment with doxorubicin, as was the antiapoptotic *YWHAH*.

Conclusion: Despite a correlation of the number of differentially regulated genes to the tumor grading and to a lesser extent histological subtype, the expression patterns varied strongly; however, especially among high grade tumors the responses of selected apoptosis genes were similar. The predescribed low clinical response rates of low grade liposarcoma to doxorubicin correspond to our results with only little changes on gene expression level and also divergent findings concerning the up- and down-regulation of single genes in the different sarcoma samples.

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