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Modulation of differentiation in choriocarcinoma cells also modulates adhesion to endometrial cells in an *in-vitro*-model

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Choriocarcinoma cells are the malignant equivalent of the trophoblast and, therefore, provide a model to study certain aspects of the regulation of trophoblast differentiation and invasion. Comparative studies of normal and malignant trophoblast cells may give valuable insight into mechanisms involved in the control of invasion and their defects in malignant cells, in particular since even the normal counterpart does already exhibit a degree of invasion that, however, is limited.

We are interested in the relation of trophoblast invasiveness to cell differentiation and have, therefore, studied differentiation responses of choriocarcinoma cells (cell lines BeWo, Jeg 3, JAr) in correlation with cell-cell-attachment reactions forming a prerequisite for invasion.

The endometrial epithelial cell line RL 95-2 was used as a model for a physiological adhesion substrate for trophoblast cells. Adhesion of choriocarcinoma cell spheroids to confluent monolayer cultures of RL 95-2 was examined as described previously (John et al., Cancer Res Clin Oncol 117, 1991, S 56; In Vitro, in press). In experiments with untreated cells adhesion of about 60 to 80% of choriocarcinoma cell spheroids occurred within one hour. This interaction was reduced in the presence of extracts of the respective choriocarcinoma cells and/or of RL 95-2. The presence of heparin or chondroitin-sulfate decreased spheroid attachment by about 80%. Exposure of choriocarcinoma cells to effectors of differentiation (cAMP; retinoic acid, methotrexate, phorbol-12-myristate-3-acetate) resulted in increased secretion of the differentiation markers chorionic gonadotropin (ranging from 2-fold to 100-fold), placental lactogen, and pregnancy-specific glycoprotein b1. In contrast, rates of spheroid adhesion were decreased by up to 70%.

These results suggest that, in this system, differentiation and at least certain elements of invasive and metastatic behaviour, i. e. adhesion to host cells, are correlated inversely.

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