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Z 23 INDUCTION OF DIFFERENTIATION IN CHORIOCARCINOMA CELLS MODULATES ELEMENTS OF INVASIVENESS IN *IN-VITRO*-MODELS

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Differentiation therapy of cancer usually focusses on the widespread inverse correlation between proliferative activity and differentiation. Little is known, however, about the relationship between invasive behaviour and differentiation of tumor cells. We have examined differentiation responses of choriocarcinoma cells (cell lines: BeWo, Jeg-3, JAr) in correlation with different elements of invasiveness, i.e. cell-cell and cell-matrix adhesion, and penetration into matrix models.

Exposure of choriocarcinoma cells to effectors of differentiation (retinoic acid, RA; dibutyryl-cAMP, cAMP; methotrexate, MTX; phorbol-12-myristate-3-acetate, PMA) increased the production of the differentiation marker chorionic gonadotropin (2-fold to 100-fold). Cell-cell attachment (a prerequisite for invasion) to the endometrial epithelial cell line RL 95-2 (used as a model for a physiological cell adhesion partner for trophoblastic cells) was decreased by up to 70%. Attachment to components of the extracellular matrix (fibronectin, laminin, collagens I and IV, basement membrane-like Matrigel) was also reduced (exceptions are only seen with some matrix components in Jeg-3 cells).

Invasiveness was assayed in transwell chambers with gels of collagen I or Matrigel. Induction of differentiation had heterogeneous effects on the invasion potential of the cells, obviously depending on the signal transduction pathway affected by the drugs: While invasion into collagen as well as into Matrigel was reduced by MTX and cAMP it was increased by RA and PMA.

These results suggest that only some elements of the process of invasion (cell-cell and cell-matrix adhesion) are inversely correlated with differentiation. Invasive behaviour, however, is modulated in a more complex way depending on the signal transduction pathway affected by inducers of differentiation.

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