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ABSTRACTS

Th-153 MODULATION OF DIFFERENTIATION ALTERS ADHESIVENESS AND INVASIVENESS OF CHORIOCARCINOMA CELLS

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During blastocyst implantation human trophoblastic cells undergo a differentiation program in preparation for the various functions they have: in early pregnancy adhesion to the uterine epithelium, penetration of the basement membrane, and invasion into the endometrial stroma; later on production of pregnancy hormones and embryo nutrition dominate.

We are studying, in vitro, how adhesiveness and invasiveness of human trophoblastic cells are correlated with differentiation using choriocarcinoma cell lines (BeWo, JAr, JEG-3) as a model. Cells were treated with modulators of differentiation: retinoic acid (RA), methotrexate (MTX), dibutyryl cyclic AMP (cAMP) and phorbol-12-myristoyl-13-acetate (PMA). Differentiation was monitored by measuring secretion of human chorionic gonadotropin (hCG). Two aspects of adhesiveness were tested: (i) cell-cell-adhesion of multicellular choriocarcinoma spheroids to monolayers of an uterine epithelial cell line (RL95-2); (ii) cell-matrix-adhesion of single cells to components of the extracellular matrix (ECM). Invasiveness was measured in a Transwell™ chamber assay with Matrigel™ as a barrier.

All tested modulators stimulated differentiation in terms of increased secretion of hCG. In parallel, adhesion to endometrial cells was always reduced, whereas adhesion to ECM components was not altered. Invasiveness, in contrast, could be affected in both directions depending on the modulator used: e.g. RA and PMA increased, MTX and cAMP decreased invasion of JAr cells.

These results suggest an inverse correlation between differentiation of trophoblastic (choriocarcinoma) cells and their adhesiveness for host cells. The relation between differentiation and matrix penetration appears to be more complex, possibly depending on the pathway of signal transduction that is influenced by the used modulators of differentiation.

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