

Joint Meeting of the

## Deutsche Gesellschaft für Zellbiologie and the Dutch Society for Cell Biology

### Main Topics

Protein folding — Endothelium — Cytoskeleton — Interphase cytogenetics —  
Image analysis — Extracellular matrix — Biomineralization — Lipoprotein cell  
interactions — Cilia and flagella — Nucleus — Apoptosis — Ion channels —  
Smooth muscle cell — Peroxisomes

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#### 43 Modulation of differentiation alters the adhesive behaviour of choriocarcinoma cells

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Trophoblast cells mediate the first steps of blastocyst implantation into the uterus, i.e. attachment to the uterine epithelium and invasion into the endometrial stroma. During implantation and subsequent placentation the trophoblast undergoes a differentiation program that starts and stops the physiological invasive behaviour of these cells. One aspect of this invasive potential are adhesive properties of trophoblast cells: they have to be able to attach to (i) uterine epithelial cells and (ii) components of the extracellular matrix (ECM) in basement membranes and in the stroma of the uterus.

We have examined the correlation between differentiation and adhesive properties of trophoblast cells using as a model choriocarcinoma cell lines (BeWo, JAr, Jeg-3), which have retained trophoblast-specific characteristics of differentiation like the production of peptide and steroid hormones. The cells were treated with chemical modulators of differentiation: Retinoic acid (RA), methotrexate (MTX), dibutyl cyclic AMP (cAMP) and phorbol-12-myristoyl-13-acetate (PMA). Differentiation was then monitored by measuring the secretion of chorionic gonadotropin (hCG). Adhesive behaviour was tested in two systems: (i) cell-cell adhesion of multicellular choriocarcinoma spheroids to monolayers of the endometrial cell line RL95-2; (ii) cell-matrix adhesion of suspended single cells to isolated components of the ECM (fibronectin, laminin, collagen I and IV) and to the complex basement membrane-like matrix Matrigel.

Differentiation in terms of increased secretion of hCG was stimulated with all effectors in all three cell lines (up to 7x for spheroids, up to 40x for monolayers). Under the same conditions the cell-cell adhesion to endometrial cells was reduced up to total inhibition of attachment for BeWo and JAr cells, and up to 50 % for Jeg-3 cells. Adhesion to ECM-components was more or less reduced on all substrates in BeWo and JAr cells. Reduction was most pronounced on fibronectin and Matrigel. In Jeg-3 cells the results were more heterogeneous. Adhesion to Fibronectin can be reduced by MTX, but stimulated by RA or PMA.

These results suggest an inverse correlation between differentiation of choriocarcinoma cells and their adhesive properties as relevant for invasion.

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