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55 Mechanical/structural signaling may direct differentiation of choriocarcinoma cells on extracellular matrix.

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Human choriocarcinoma cells express trophoblast-specific differentiation markers and are, therefor, a useful model to study the the differentiation potential of tumor cells and its relevance for malignancy. When BeWo choriocarcinoma cells are maintained on different forms of extracellular matrix, expression of the differentiation marker chorionic gonadotropin (hCG) was stimulated much more (up to 5-fold) when cells were grown on flexible matrix gels as compared to cells grown on rigid/non-flexible substrates of the same chemical composition (coated plastic). This difference was accompanied by a change in morphology from cell monolayers (on coated plastic) to cell spheroid-like aggregates of more rounded cells (on matrix gels). Comparable results were obtained when cells were grown on artificial matrix gels consisting of glyoxyl agarose to which different combinations of matrix molecules were crosslinked covalently. A similar correlation was also observed during experimental modulation of culture morphology of cells grown on plastic: In response to reduction of substrate adhesiveness (plastic coated with different concentrations of poly-HEMA) the cells assumed a more rounded shape and formed aggregates attached to the support. Concomitantly the secretion of hCG was increased up to the levels obtained on matrix gels. Piling up of cells did not seem to be the cause for this difference: Expression of connexins and of E-cadherin was not correlated with hCG production (attached cell spheroid-like aggregates as compared to spheroids in suspension culture and to cell monolayers). Conclusions: A rounded morphology combined with polar attachment to a substrate facilitates cell differentiation. Flexibility/malleability of matrix substrates appears to be even more critical in this respect than its chemical composition, i.e., the type of matrix receptors involved in attachment, thus pointing to a central role of the cytoskeleton and of architecture in differentiation.

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ABSTRACTS

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