PARAMETERS CORRELATED WITH DIFFERENCES IN INVASIVENESS OF TROPHOBLAST AND CHORIOCARCINOMA CELLS.

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During embryo implantation and placentation trophoblast cells undergo a differentiation program involving modulation of invasiveness and acquisition of endocrine and transport functions thus yielding various subpopulations of cells. We are reporting here on studies of correlations between trophoblastic differentiation and invasiveness as well as cellular activities that may be involved in modulating invasion of trophoblastic cells.

JAR choriocarcinoma cells, a malignant counterpart of human trophoblast, were treated *in vitro* with retinoic acid (RA), methotrexate (MTX), dibutyryl-cyclic AMP (cAMP), and phorbol-12-myristoyl-13 acetate (PMA), and differentiation was monitored by measuring the production of human chorionic gonadotropin (hCG). Invasiveness of treated cells was assayed *in vitro* using porous membranes (pore size = 8 µm) covered with a layer of the basement membrane-like extracellular matrix (Matrigel). MTX and cAMP reduced invasion rates while RA and PMA, in contrast, increased invasiveness. These differences could not be correlated with the activity of proteases, adhesion to ECM components, or cell motility. Our data do show, however, an inverse correlation between expression of ECM-molecules and invasiveness, suggesting a role of ECM production in controlling invasion.

A systematic search was started for correlation of altered gene activity with differences in invasiveness, using DDRT-PCR. Trophoblast cells with different invasive potential, i.e. JAr cells treated with PMA and cAMP as well as normal human trophoblast cells isolated from first trimester and term placentae were compared. Minor differences were seen between JAr cells treated or not with cAMP or PMA. However, differences were considerable between invasive (first trimester) and noninvasive (term) trophoblast cells and between normal and malignant (JAr) trophoblast cells. These data are used in a search for molecules putatively regulating invasiveness in this system.

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