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INTERACTION OF TROPHOBLAST AND OF TUMOR CELLS WITH ENDOMETRIAL FRAGMENTS IN ORGAN CULTURE

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The uterine epithelial lining shows a property which is unusual for an epithelium: after proper hormonal conditioning it can enter a special physiological state("receptive state") during which attachment of trophoblast to its apical surface is possible and may be followed (in most species) by invasion. It is hoped that the possibility to manipulate this "receptivity" via its steroid hormone dependency may help to define factors involved in the regulation of invasive processes.

We have previously reported on an endometrial organ culture system which apparently allows rabbit endometrium to develop at least many major characteristics of the "receptive state" in vitro (C.T.O.C. Meeting, Milano 1983; Eur.J.Cell Biol. 33, Suppl. 5, 17, 1984). When implantation stage rabbit blastocysts are confronted with these endometrial fragments in vitro, the syncytiotrophoblast can attach to the uterine epithelium and invade it, provided that the culture system allows to maintain a close physical contact for prolonged periods of time (C.T.O.C. Meeting, Noordwijkerhout 1984). The light and electron microscopical details of attachment and invasion in this system are very similar to what is observed in vivo.

Whether or not this "receptivety" involves any specificity for trophoblast is being tested in a recent series of experiments on confrontation of the endometrial fragments with tumor cell aggregates. It has previously been reported

that certain tumor cells (Walker carcinosarcoma, Harding-Passey melanoma, Flexner-Jobling carcinoma, and others) can invade the endometrium of the mouse and rat when introduced into the uterine lumen during the "receptive period" in vivo (Short and Yoshinaga 1967; Wilson and Potts 1970; Smith and Hartman 1974; for earlier work cf. Cowell 1972).

However, morphological details of invasion and induction of a decidual reaction were varyable with the different types of tumor cells. The mouse and rat system may not be optimal for such experiments since the uterine epithelium is known to be very fragile and to degenerate easily even after slight mechanical alteration, in these species.

In our recent experiments, precultured fragments of rabbit endometrium were confronted with MO_4 mouse fibrosarcoma cell aggregates according to the model system developed by Mareel et al. During primary confrontation on a semi-solid agar medium, attachment of tumor cell aggregates to the epithelium was only weak and most of the attached tumor cells dissociated from the surface of the endometrial fragments during the following culture in liquid medium on a gyratory shaker. In contrast to trophoblast, tumor cells never invaded the tissue through a primarily intact epithelium, but were successful in invading if confronted with the stromal side of uterine explants. Additional experiments with other tumor cell lines will have to be performed before a more definitive answer can be given to the question whether the state of "receptivity" of the epithelium for attachment and invasion is indeed specific for trophoblast in our rabbit endometrial model system.

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