Endometrial organ culture: development of an in-vitro model for embryo implantation

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Embryo implantation involves the astonishing phenomenon of contact formation between the apical parts of two epithelia, i.e. trophoblast and uterine epithelium, starting with superficial attachment and formation of intercellular junctions and followed by penetration of the trophoblast through the epithelium. In continuation of morphological, histochemical and biochemical studies and of *in-vivo* experiments on the mechanisms of implantation initiation, we are now trying to develop an *in-vitro* model for trophoblast attachment and invasion. The modeluses confrontation cultures of three dimensional endometrial fragments plus blastocysts. The general design of the system is related to that developed by Mareel et al. [Virchows Arch. B. Cell Pathol. **30** (1979) 95] in which tumor cell invasion is studied by *in-vitro* confrontation with precultured chick heart fragments. — Our first series of experiments has concentrated on the formation and the maintenance, in-vitro, of three dimensional fragments of endometrium which are completely covered by uterine epithelium. These organotypic fragments will finally be confronted with the trophoblast of implantation stage blastocysts. Endometrium was obtained from pseudopregnant rabbits at 5 d after injection of HCG and was cultured on a gyratory shaker. Light and electron microscopical studies revealed that the epithelium usually grew over the cut surface of the stroma completely during a 2 d incubation period. At the former wound, the epithelium was at first flat but nevertheless well polarized, and it later grew in height. Even after a total incubation period of 4 d there was usually no central necrosis in the stroma. However, there was evidence for shedding of uterine epithelial cells, particularly those located superficially, if no hormones were added to the medium. On contrast certain hormonal regimens (progesterone, estradiol-17β) were found to maintain, *in vitro*, a superficial epithelium which showed most morphological criteria typical for the late preimplantation phase including e.g. formation of symplasms by cell fusion. First results on co-culture of blastocysts with the endometrial fragments showed a remarkable degree of development of the embryos. — This model may allow us to study cell biological changes in the uterine epithelium which form an essential element of the "receptive state" during which the trophoblast can succeed in attaching to the otherwise non-adhesive surface of the epithelium, and in penetrating it.

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