8 The Role of Blastolemmase in Implantation Initiation in the Rabbit

Hans-Werner Denker

I. Introduction

Implantation of the mammalian embryo in the uterus involves the formation of cellular contact between embryo and maternal tissues. The molecular–biological mechanisms of this process are poorly understood. Systematic investigations in the rabbit have provided evidence that certain enzymes, particularly a peculiar trophoblast-dependent proteinase, play an interesting role.

II. Results

Implantation in the rabbit follows the central type. At the time of attachment, i.e., 7 days postcoitum, the blastocyst is considerably expanded (approximately 5 mm in diameter); it is oriented, by an unknown mechanism, with the embryonic disk facing the mesometrial endometrium and the abembryonic trophoblast facing the antimesometrial endometrium. Up to this stage, extracellular blastocyst coverings are still interposed between trophoblast and uterine epithelium. These blastocyst coverings are equivalent to the zona pellucida that has been dissolved in earlier stages; they are derived from secretions of the tube, the uterus, and the trophoblast (Denker and Gerdes, 1979). According to histochemical investigations, their composition is comparable to that of epithelial mucins: protein backbone and carbohydrate side chains with sulfate ester groups and terminal sialic acid (Denker, 1970). A particularly well-developed glycocalyx is present at the surface of the uterine epithelium and shows a somewhat similar composition.

Contact between trophoblast and uterine epithelium is first established in the abembryonic–antimesometrial region. It is preceded by an increase in stickiness of blastocyst coverings and uterine epithelial surface, followed by dissolution of the barrier formed by the blastocyst coverings. This process may involve enzymatic changes of the glycoprotein substances. In fact, considerable activity of various glycosidases as well as exo- and endopeptidases is demonstrable histochemically at these sites during initiation of implantation. Of particular interest is a peculiar endopeptidase (proteinase) activity which is trophoblast-dependent and which appears exactly at the time (and the site) of antimesometrial implantation and which disappears immediately thereafter (Denker, 1971). This enzyme is called blastolemmase. As shown by experiments with various proteinase inhibitors *in vitro*, blastolemmase is closely related to trypsin. Substrate specificity, however, is more re-

Hans-Werner Denker • Abteilung Anatomie der RWTH, D-5100 Aachen, West Germany.

stricted: arginyl bonds are much more easily hydrolyzed than lysyl bonds, and hydrolysis rates are strongly influenced by the type of amino acid present in subsite positions P_2 and P_3 adjacent to the arginyl residue (P_1) (Denker and Fritz, 1979).

Proteinase inhibitors that inhibited blastolemmase effectively *in vitro* (such as aprotinin = Trasylol, antipain, NPGB) were administered intrauterally *in vivo* at 6 days 12 hr pc, i.e., 12 hr before the time of implantation initiation (Denker, 1977). This treatment resulted in blockage of dissolution of blastocyst coverings, which remained interposed between trophoblast and uterine epithelium so that attachment was impossible. The unattached blastocysts continued to expand, and as a result the undissolved blastocyst coverings ruptured. In such places a delayed and locally restricted attachment can occur. These experiments illustrate that blastolemmase plays an important role in dissolution of the blastocyst coverings in a manner reminiscent of a hatching enzyme. The possible roles of uterine-secretion proteinases and of other enzymes of the trophoblast and the endometrium (like glycosidases) remain to be defined. Whether or not these enzymes are also directly involved in the process of formation of cellular contact between trophoblast and uterine epithelium needs further investigation.

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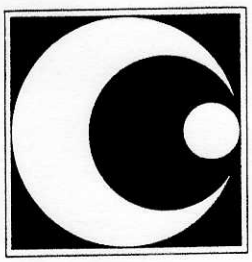
Edited by
Stanley R. Glasser
and
David W. Bullock
Baylor College of Medicine
Houston, Texas



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