Expression of plasminogen activators in human endometrial stromal cells during implantation

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To determine whether altered expression of the tissue type (tPA) and urokinase type (uPA) plasminogen activators accompanies decidualization, confluent monolayers of endometrial stromal cells from predecidualized human endometria were incubated for 3 days (d) in a defined medium containing 10-8M E2, or 10-7M medroxyprogesteron-acetat (MPA), or E2+MPA, or 0.1% ethanol as control. Detected by specific ELISAs, added MPA reduced uPA levels by 19% and tPA by 33%. Even greater reductions were seen in response to E2+MPA (74% for uPA and 49% for tPA). A chromogenic assay was used to discriminate between the amounts of fibrin-independent PA activity (uPA) and fibrin-dependent activity (tPA) in the stromal cell conditioned medium. Two hours preincubation at 37C increased measured uPA activity under control conditions by about 20-fold, indicating that the stromal cells released uPA predominantly as catalytically inactive pro-uPA. Both uPA- and tPA activity were refractory to E2, inhibited by MPA, and synergistically inhibited by E2+MPA. Interestingly enough, E2+MPA reduced the activities of secreted uPA and tPA to nondetectable levels despite significant immunogenic levels of both PAs. This preferential inhibition of activity versus antigen may reflect the action of the potent PA inhibitor, PAI-1, whose output by the cultured stromal cells is elevated by MPA and even more increased by E2+MPA.
Conclusion: During implantation, inhibition of decidual cell expressed tPA, the prime fibrinolytic agent, by the predominant steroids of pregnancy can prevent hemorrhage, whereas reduction in decidual cell derived pro-uPA can lower the paracrine supply to specific trophoblast cell uPA receptors and thereby limit trophoblast invasiveness.