Integrins $\beta_5$, $\beta_3$ and $\alpha_v$ are apically distributed in endometrial epithelium

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Several adhesion molecules have been shown to occur at the surface of endometrial cells. One of these is the integrin $\alpha_v$ subunit which associates with various $\beta$ chains including $\beta_5$. We demonstrate the presence of integrin $\beta_5\pi$ polypeptide in human endometrial epithelial cells throughout the menstrual cycle using immunocytochemistry with monospecific antibodies, and at the mRNA level by thermal amplification from endometrial cDNA. Integrin $\beta_5$ is also found in a population of bone marrow-derived cells. A notable feature of the distribution of the $\beta_5$ subunit in the glandular and luminal epithelium is its apical localization, which may suggest an involvement in implantation. However, no evidence was found for regulated expression of epithelial $\beta_5$. In mouse, the $\beta_5$ subunit is found at both the apical and basal surface of epithelial cells and expression is essentially oestrous cycle-independent. Comparisons are made in both species with the distribution of the $\alpha_v$ and $\beta_3$ subunits which also localize to the apical epithelium.

Key words: cell surface/decidua/embryo implantation/endometrium/integrin

Introduction

The endometrial epithelial cell surface is the first point of stable contact between the blastocyst and maternal tissue. Receptivity to implantation appears to be controlled by the endometrial luminal epithelium (Glasser and Mulholland, 1993; Tabibzadeh and Babaknia, 1995). Thus it is important to examine the cell surface composition of endometrial epithelium; the presence of adhesion and anti-adhesion molecules may indicate a function in intercellular interaction in early pregnancy. We and others have demonstrated the presence of integrins (Lessey et al., 1992; Tabibzadeh, 1992; Klentzeris et al., 1993; Aplin et al., 1994; Albers et al., 1995; reviewed in Bronson and Fusi, 1996) and other adhesion molecules (Lindenberg et al., 1988; Kimber et al., 1993; Behzad et al., 1994; Fukuda et al., 1995) in endometrial epithelium in human and mouse. MUC1, an apically disposed epithelial cell surface molecule with anti-adhesion properties, is expressed in the endometrium in both these species (Braga and Gendler, 1993; Hey et al., 1994, 1995). Integrin $\beta_3$, which associates with $\alpha_v$, to form a multifunctional receptor for several extracellular arginine–glycine–aspartic acid (RGD)-containing ligands including fibronectin, vitronectin, fibrinogen and osteopontin (Hynes, 1992; Felding-Habermann and Cheresh, 1993), shows an interesting pattern of regulation in human endometrial glandular epithelium, with onset of expression at approximately day 19 of the cycle (Lessey et al., 1992). Since the $\alpha_v$ subunit is present in the same cells, but appears not to share this pattern of regulation (Lessey et al., 1992), it appears likely that other $\beta$-subunits capable of association with $\alpha_v$ may also be expressed. In this study we have examined the expression of integrin $\beta_5$, which associates with $\alpha_v$, to form an RGD-dependent receptor for fibronectin, vitronectin or osteopontin (Felding-Habermann and Cheresh, 1993; Liaw et al., 1995). We show that this integrin is present in the luminal epithelium in both human and mouse endometrium at the time of implantation.

Materials and methods

Animals

MF1 mice (Harlan OLAC, Bicester, UK) were kept in a controlled environment with a cyclic photoperiod of 12 h light followed by 12 h darkness and provided with food and water ad libitum. Ovariectomized mice were rested for 10 days then injected with vehicle (corn oil) or 100 ng oestradiol benzoate daily for 2 days followed by 2 days' rest. Oestrogen-primed animals were then divided into three groups. The first group received 100 ng oestradiol benzoate daily for 4 further days. The second group received 500 ng progesterone daily for 4 further days. The third group received 500 ng progesterone daily for 3 days, then 500 ng progesterone with 10 ng oestradiol on the fourth day. They were killed by cervical dislocation 16 or 18 h after the last injection. Pregnant uterine horns were taken from naturally-mated MF1 female mice. The animals were paired with MF1 male mice and left overnight. Mating was assumed to occur at approximately midnight. The following morning successful mating was confirmed by the presence of a vaginal plug. This day was designated as day 1 of pregnancy.

The uterine horns were trimmed of fat, removed and placed in Hank's Balanced Salt Solution (HBSS; Gibco BRL, Paisley, UK). Tissue from three different animals was used to study each day of pregnancy, the oestrous cycle and there were also three different