

Control of Growth and Differentiation of the Endometrium: The Role of Tissue Interactions

ROBERT M. BIGSBY

Indiana University School of Medicine, Indianapolis, Indiana 46202, USA

ABSTRACT: Early work with neonatal mice showed that estrogen receptor-negative uterine epithelium responded to estrogen treatment. Since the underlying mesenchymal cells were estrogen receptor-positive, it was suggested that these cells mediated the hormonal response through elaboration of a paracrine factor. Cell culture work showed that mesenchymal cells produced soluble factors that stimulate uterine epithelium, but hormonal regulation was absent or minimal. The paracrine hypothesis of estrogen action has been proved by the use of tissue recombination studies in which epithelium from estrogen receptor-alpha knockout mice was combined with wild-type mesenchyme; estrogen stimulated the ER α -negative epithelium if the underlying stromal cells were receptor-positive. Also, it is hypothesized that there is a reciprocal paracrine interaction during stimulation with progesterone and estrogen. Accordingly, under progesterone dominance, the epithelium elaborates factors that direct the underlying stroma to proliferate when estrogen is administered. Although this hypothesis needs further testing, it has been shown that the uterine epithelium is required for stromal responsiveness to hormones. The question arises: What are the factors that mediate the effects of the steroid hormones in the uterus? Several peptide growth factors are regulated by estrogen and/or progesterone. Use of knockout animals will allow a determination of the role that these factors play in the uterus. However, ablation of many of these growth factor genes has proved lethal to the newborn animals, making it impossible to study hormonal effects using standard techniques. Tissue xenograft and tissue recombination studies offer a means of defining the role of specific growth factors in uterine physiology.

KEYWORDS: tissue interactions; paracrine factors; cell proliferation; estrogen; progesterone; tissue recombinations; xenograft; gene knockout

One of the hallmarks of endometriosis is the inclusion of endometrial stroma in the ectopic tissue implant. Is this merely a diagnostic tool for pathologists or does it point to a biologically important aspect of the disease process? Endometriomas are responsive to hormonal changes, but the hormonal effects are not always identical to those occurring in the normal endometrium. Do the hormonal responses of endometrioma tissues derive from an interaction of the stromal and epithelial tissues and

Address for correspondence: Robert M. Bigsby, Ph.D., Department of Obstetrics and Gynecology, Indiana University School of Medicine, 975 West Walnut Street (IB3560), Indianapolis, IN 46202-5121. Voice: 317-274-8970; fax: 317-278-2884.
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