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Epithelial–Stromal Tissue Interaction in Paramesonephric (Müllerian) Epithelial Differentiation

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Abstract

During organogenesis, the middle to caudal portion of Müllerian epithelium differentiates into uterine and vaginal epithelia in females. Functional differentiation of uterine and vaginal epithelia occurs in adulthood, and is regulated by 17β-estradiol (E_2) and progesterone. In this report, the roles of mesenchyme/stroma in differentiation of uterine and vaginal epithelia were studied in tissue recombination experiments. At birth, Müllerian epithelium was negative for uterine and vaginal epithelial markers. Tissue recombinant experiments showed that uterine and vaginal gene expression patterns were induced in neonatal Müllerian epithelium by the respective mesenchymes. Differentiated adult uterine and vaginal epithelia did not change their original gene expression in response to heterotypic mesenchymal induction. In the adult vagina, E_2 induced expression of involucrin, a CCAAT/enhancer-binding protein β and cytokeratin 1 via estrogen receptor α (ERα). Tissue recombination experiments with wild-type and ERα knockout mice demonstrated that epithelial gene expression is regulated by E_2 via epithelial–stromal tissue interactions. Uterine/vaginal heterotypic tissue recombinations demonstrated that functional differentiation of uterine and vaginal epithelia required organ-specific stromal factors. In contrast, stromal signals regulating epithelial proliferation appeared to be nonspecific in the uterus and vagina.

Keywords

uterus; vagina; cervix; tissue recombination; cornification; estrogen receptor α; progesterone receptor; cytokeratins; proliferation

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