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The role of the epithelial sodium channel (ENaC) in cervical mucus hydration

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Keywords

Cystic Fibrosis Transmembrane Conductance Regulator; Macaca mulatta; Epithelial Sodium Channels; Amiloride; Cervix Mucus; Cervix Uteri; Menstrual Cycle; Contraceptive Agents; Estradiol; Fertility; Steroids

Abstract

OBJECTIVE: The production of cervical mucus plays a crucial role in regulating fertility, with hormonal regulation of ion channels, such as the epithelial sodium channel (ENaC), being a key factor. This study aims to enhance our understanding of the role ENaC plays in mucus production and hydration.

MATERIALS AND METHODS: Differentiated endocervical cells from the Rhesus Macaque (Macaca mulatta) were primed with estradiol (10nM) to mimic the peri-ovulatory phase of the menstrual cycle. Cultures were subsequently treated with amiloride, an ENaC inhibitor, at concentrations of 10uM and 100uM, or vehicle alone. Using particle-based tracking microrheology (PTMR), we analyzed the thermal motion of fluorescently tagged particles to determine viscoelastic properties of mucus at 24- and 48-hour timepoints.

RESULTS: Our results show a dose-dependent decrease in viscosity of mucus produced by endocervical cells in response to amiloride treatment compared to vehicle-only controls. At 48 hours, we saw significantly decreased average viscosity (0.03 Pa·s) in cultures treated with amiloride (100uM) as compared to control (0.6 Pa·s) (p=0.023).

CONCLUSIONS: Our previous studies have shown that sex steroids regulate ENaC expression. The current findings, which demonstrate that inhibition of ENaC leads to a decrease in mucus viscosity, suggest that ENaC regulation is involved in the cycle-dependent changes of cervical mucus, along with other ion channels such as the cystic fibrosis transmembrane conductance regulator (CFTR). This study further supports the important role of epithelial ion channels in fertility changes in the cervix and highlights their potential as targets for the development of non-hormonal contraceptives.