RECAPITULATING HUMAN MENOPAUSAL VAGINAL TISSUE WITH AN OVARIECTOMIZED MOUSE MODEL

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Background: All women experience menopause as they age due reduced estrogen. The resulting vaginal environment fosters debilitating vaginal symptoms. Current treatment options anecdotally improve symptoms, but rectifying mechanisms are largely understudied. To understand mechanisms behind treatments and develop new therapies, we developed and characterized a reliable model for evaluating menopausal vaginal tissue.

Materials/Methods: We performed bilateral ovariectomies (OVX) on 9-week-old CD1 female mice using naïve and sham-operated mice as controls (n=4-5). After one month, we harvested and weighed the reproductive tract. Vaginal tissue sections were stained using H&E, Picro-sirius red, HA binding protein, and immunohistochemistry for ERα, CD45, F4/80, and CD44. RNA was isolated from snap frozen vaginal tissue, and RT2 Profiler arrays were used to evaluate inflammation, extracellular matrix (ECM), and estrogen signaling. ANOVA with Dunnett's post-hoc were used to determine statistical significance ($p < 0.05$).

Results: The uterine to body weight ratio, representing circulating estrogen, featured an 80% decrease in OVX compared to sham and naïve mice. We found significantly thinner epithelium in OVX compared to controls. Estrogen signaling differed as expected; while vaginal ERα staining was slightly elevated in OVX, this increase did not reach statistical difference between groups. The inflammation profile was disrupted following OVX, and both vaginal CD45 and F480 were significantly reduced. The ECM profile and collagen turnover was altered following OVX. While we found no difference in total vaginal HA between groups, we observed differential HA localization and decreased CD44 expression in OVX mice.

Conclusions: We have evaluated a bilateral ovariectomy mouse model, which recapitulates many features observed in human post-menopausal vaginal tissue. We further found reduced estrogen results in decreased basal vaginal inflammation which may manifest in the lower defense mechanisms that post-menopausal women suffer from. Further studies using this mouse model will allow for advancement in women's vaginal health treatments.

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