Stromal estrogen receptor-alpha is involved in the development of lower urinary tract dysfunction.

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ABSTRACT
Introduction: Aging men exhibit a shift in hormone levels which contribute to the development of lower urinary tract dysfunction (LUTD). We recently determined that *in utero* and lactational exposure to the persistent environmental toxicant, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), exacerbates voiding dysfunction in the testosterone (T) and 17b-estradiol (E2) model of LUTD. It was also demonstrated that estrogen receptor-alpha (ER-α) was necessary for the development of LUTD in C57Bl/6 male mice. The objective of this study was to determine if stromal ER-α was necessary for the development of LUTD.
Methods: To determine the specific role of estrogen receptor-alpha (ER-α) in prostatic stroma we used stromal specific smooth muscle-cre (B6.Cg-Tg(TgIn-cre)1Her/J) mice crossed to ER-α floxed mice, which deleted prostatic stroma ER-α. These mice were exposed *in utero* to TCDD at embryonic day 13.5 (or corn oil), then in adulthood at six weeks were treated with T and E2 or sham using slow release subcutaneous implants. To assess voiding behavior, we utilized void spot assays (VSA) each week for four weeks following hormone treatment. Mice were necropsied after the 4th VSA to assess the bladder and prostate.
Results: We observed decreased bladder mass and void dribbling in the stromal ER-α knockout in comparison to wild type for the TCDD and hormone treated groups.
Conclusion: These findings suggest that stromal ER-α plays a key role in the development of lower urinary tract dysfunction (LUTD) in this 2-hit model of LUTD. To further investigate the role of ER-α in other cell types future work will use epithelial-specific cre: B6.Cg-Shh $^{tm1(EGFP/cre)Cit}$/J mice.