Dissecting the Role of Epithelial vs. Stromal Estrogen Receptor α in Lower Urinary Tract Dysfunction

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Background

Aging men experience Benign Prostatic Hyperplasia associated with Lower Urinary Tract Symptoms (LUTS) as a result of pathological changes in the prostate which are attributed to an age-related increase in the ratio of estradiol to testosterone has been shown to be associated with lower urinary tract dysfunction in mice.

Our group and collaborators have shown that in utero and lactation exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) sensitizes mice treated with testosterone (T) and 17β-estradiol (E2) to voiding dysfunction which leads to increased bladder volume.

Our group has also shown ERα to be essential in the progression of lower urinary tract dysfunction [3].

Objective and Hypothesis

ERα has been found in the prostatic epithelium and stroma. Although we have previously established the role of systemic ERα in LUTD progression, we have not determined what cell compartment plays a role in disease progression.

Objective: The objective of this study was to determine the respective roles of epithelial and stromal ERα in the progression of LUTD induced by testosterone and estradiol or their combination with in utero TCDD exposure in male mice.

Results

Neither Epithelial Nor Stromal Smooth Muscle Loss of ERα Significantly Affects Void Spot Count in Response to Steroid Hormone Treatment

Fig. 5. In CO/T+E2 treated mice, neither epithelial nor stromal deletion of ERα resulted in a void spot difference. Void spot counts did not significantly differ with epithelial (A) or stromal smooth muscle (B) loss of ERα in CO/T+E2 mice. Statistical significance was determined by a Student’s t test with p<0.05 accepted as significant.

Stromal Smooth Muscle Loss of ERα Results in a Significant Reduction in Void Spot Count in Response to Dioxin and Steroid Hormone Treatment

Fig. 2. Stromal deletion of ERα resulted in a significant void spot reduction in TCDD/T+E2 treated mice. Stromal loss (A) of ERα resulted in a significant reduction in void spot count, while there was no significant difference in the deletion of epithelial smooth muscle (B) to TCDD/T+E2 mice. Statistical significance was determined by a Student’s t test with p<0.05 accepted as significant. *** p<0.001

Neither Epithelial Nor Stromal Smooth Muscle Loss of ERα Significantly Affects Bladder Mass Change in Response to Steroid Hormone Treatment

Fig. 3. Bladder masses did not significantly change with either the epithelial or stromal deletion of ERα in CO/T+E2 treated mice. Bladder masses did not significantly differ with epithelial (A) or stromal smooth muscle (B) loss of ERα in CO/T+E2 mice. Statistical significance was determined by a Student’s t test with p<0.05 as significance.

Discussion

Conclusion:

- Neither stromal nor epithelial ERα deletion alleviates LUTD in CO/T+E2 mice.
- ERα deletion in multiple cell types may be necessary to reduce dysfunction in CO/T+E2 mice.
- Smooth muscle and Epithelial ERα may have different roles in the double hit model.
- TCDD/T+E2 treated mice show reduced voiding dysfunction with an epithelial deletion of ERα and decreased bladder mass with a smooth muscle ERα deletion.
- Future directions will include looking at total collagen, proliferation, and smooth muscle thickness.

References

5. GraphPad Prism was used to generate results.

Acknowledgements

This study was supported by NIH U54DK104310 and NIH R01 ES001332