

Prostate-specific *Cdh1* hemizyosity induces prostate inflammation and bladder overactivity in aged mice



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Abstract

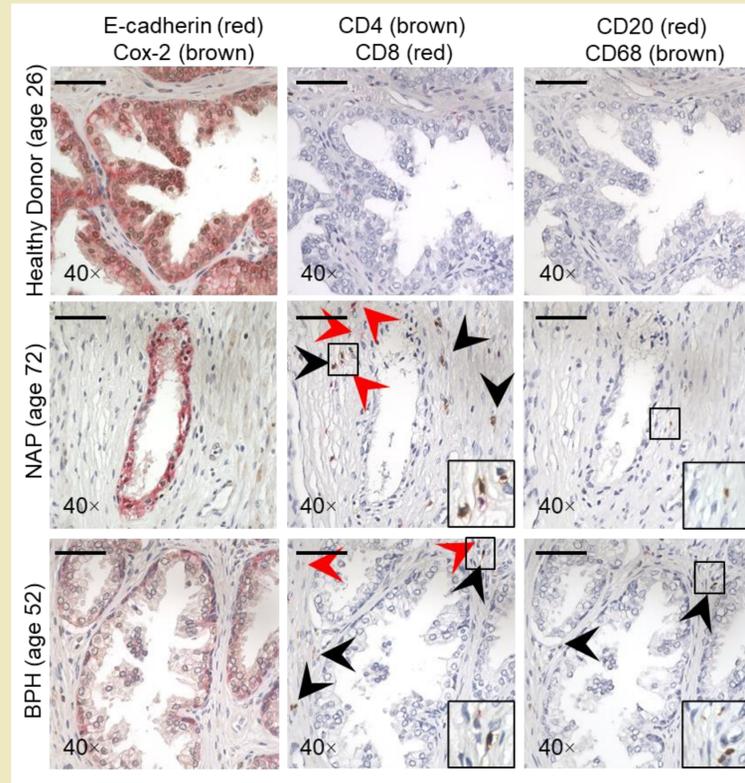
INTRODUCTION AND OBJECTIVE: Decreased adherens junction protein E-cadherin has been implicated in the development and progression of benign prostatic hyperplasia (BPH). Immunostaining has shown decreased E-cadherin to be associated with inflammation in both BPH and the aged mouse prostate. Homozygous E-cadherin deletion in murine prostate epithelium induced prostate inflammation and bladder overactivity, however, E-cadherin is reduced in BPH, but not completely lost. This study was performed to examine the impact of a reduced E-cadherin expression in combination with advanced age.

METHODS: The PSA-CreERT2 transgenic mouse strain expressing tamoxifen-inducible CreERT2 recombinase driven by a 6-kb human PSA promoter/enhancer was crossed with the B6.129-Cdh1^{tm2Kem/J} mouse to generate bigenic PSA-CreERT2/*Cdh1*^{+/-} mice. Hemizygous deletion of E-cadherin in the prostate luminal epithelial cells of male mice was induced by transient administration of tamoxifen when mice reached sexual maturity (7 weeks of age) and mice were aged to 24 mos. Immunostaining analyses and cystometry were used to determine the impact of aging and *Cdh1* hemizyosity on the prostate and bladder.

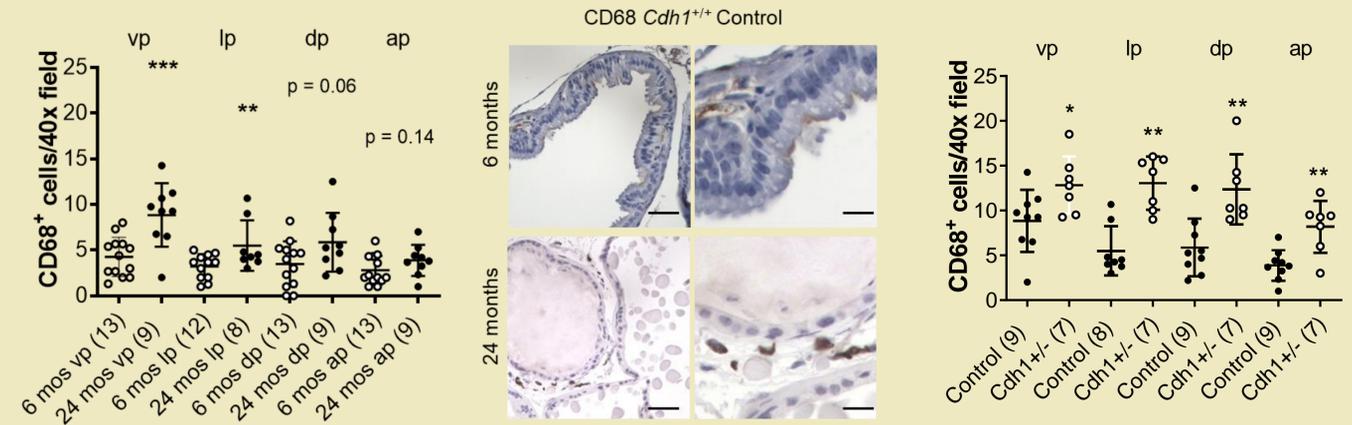
RESULTS: Aged *Cdh1*^{+/-} mice exhibited increased prostatic inflammation, stromal hyperplasia and bladder overactivity compared to age-matched controls.

CONCLUSIONS: Aged mice with prostate-specific hemizygous loss of E-cadherin developed prostatic defects and lower urinary tract symptoms similar to BPH/LUTS. This suggests that decreased E-cadherin expression may synergize with aging to induce prostatic inflammation and bladder overactivity.

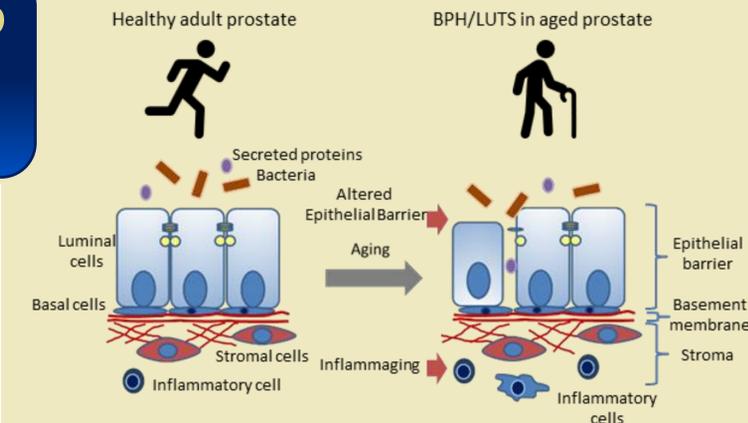
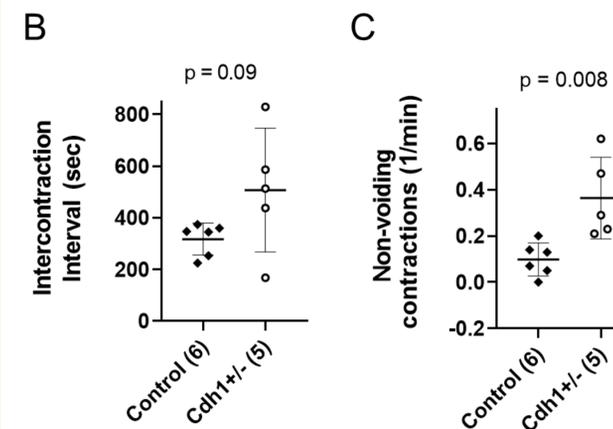
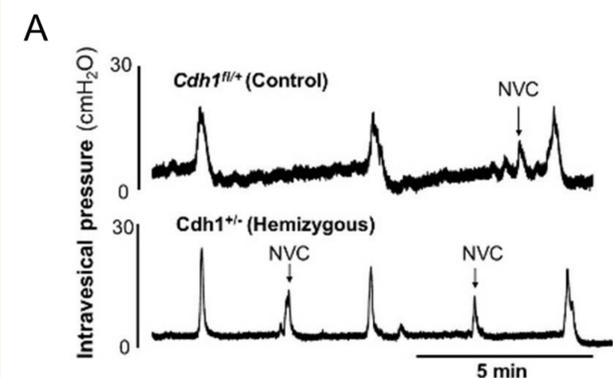
E-cadherin is decreased and prostate inflammation is increased with age and in BPH



Inflammation is increased with aging in prostates of controls and *Cdh1*^{+/-}

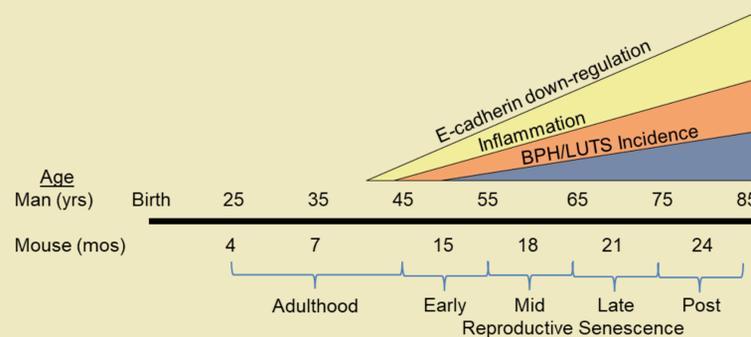


Aged *Cdh1*^{+/-} mice develop prostate inflammation and bladder activity



Aging and decreased E-cadherin synergize to induce BPH/LUTS-like changes in the prostate and bladder of mice

Aging in mice and men



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