Downregulation of cytochrome B5 reductase (CYB5R3) inactivates soluble guanylate cyclase (sGC) inducing benign prostatic hyperplasia (BPH) in humans and rodents

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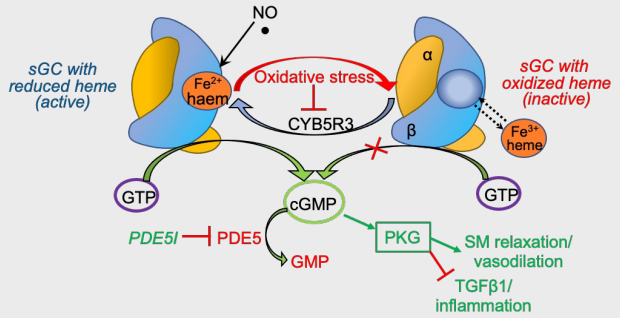
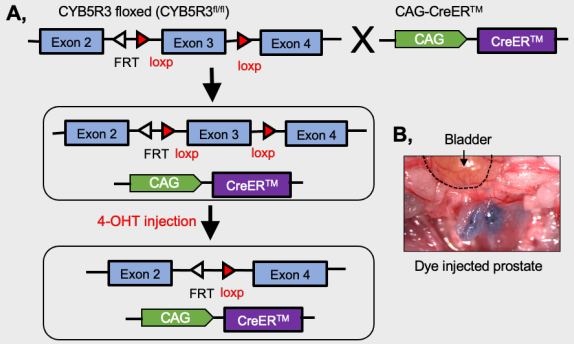
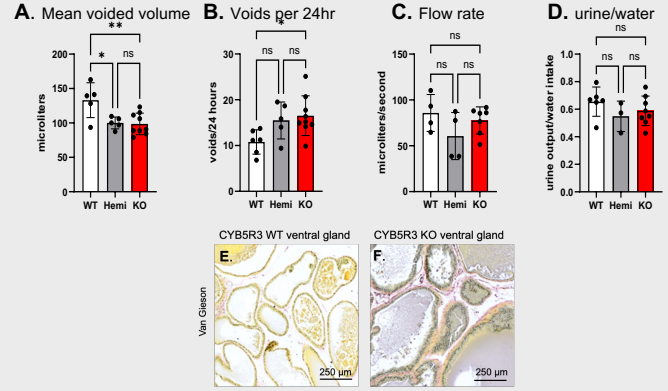
Introduction: CYB5R3 is known to be downregulated in aging and oxidative stress. Thus, the goal of this study was to determine the consequences of prostatic CYB5R3 downregulation in a mouse model and correlate these with the BPH phenotype in human prostates.



Method: Conditional CYB5R3 deletion mouse model was generated and prostate lobes injected with 4-hydroxytamoxifen (4-OHT). Mice were evaluated up to 24 weeks post injection. Voiding behaviour and histological evaluations were performed at end points. CYB5R3 expression compared in mouse and human prostate histological samples.

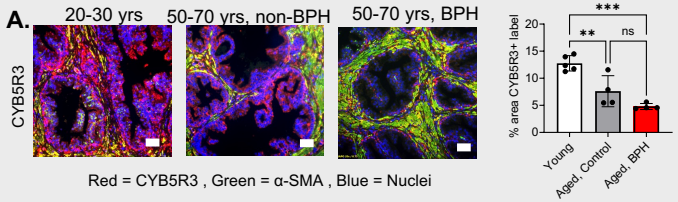


Results: CYB5R3 knockout (KO) mice showed decreased mean voided volumes and voiding frequency without changes to flow rate or urine output/water intake. Histological evaluations showed increased glandular collagen content and glandular epithelium proliferation.

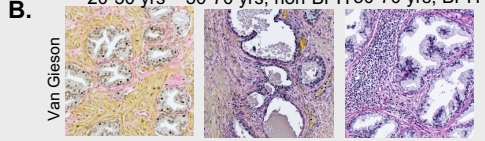


Yellow = Muscle, Pink = Collagen, Purple = Elastin, Brown/Black = Nuclei

Results: CYB5R3 expression was decreased in clinical prostate samples diagnosed with BPH verses non-BPH and correlated with increased extracellular collagen.



Red = CYB5R3 , Green = α-SMA , Blue = Nuclei



Yellow = Muscle, Pink = Collagen, Purple = Elastin, Brown/Black = Nuclei

Summary: Prostatic CYB5R3 downregulation is associated with increased collagen deposition and glandular epithelium proliferation. CYB5R3 and/or downstream pathways could represent BPH therapeutic targets for further investigation.

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