The Impact of Genetic Background on the Mouse Prostate Histological Response to Testosterone and Estradiol

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INTRODUCTION AND OBJECTIVE: Half of the men over the age of 50 suffer from varying severity of Benign Prostatic Hyperplasia (BPH), which is a condition characterized by the enlargement of the prostate. Common symptoms of BPH include frequent urination, nocturia and inability to fully empty the bladder, which significantly decrease the quality of life for those affected. Several mouse models exist to examine lower urinary tract dysfunction, but how these models recapitulate the etiology of human disease is less well understood. While C57Bl/6 mice are generally used to model disease due to the suitability for genetic modifications, genetic drift in the colony between vendors exists. This study aims to assess the differences in lower urinary tract dysfunction in C57Bl6/J and C57Bl6/NJ mice.

HYPOTHESIS: Our hypothesis is that C57Bl6/J and C57Bl6/NJ mice exhibit different phenotypes after being implanted with steroid hormone pellets.

METHODS: First, 8 week old mice were randomly separated into control and eperimental groups by sub-strain. Mice in the experimental group were implanted with 25 mg testosterone (T) and 2.5mg 17β-estradiol (E2) pellets while mice in the control group underwent surgery without implantation. Bromodeoxyuridine (BrdU) was administered in the water daily for five days post-op. Weekly void spot assays (VSA) were performed on all mice and analyzed with VoidWhizzard. The mice were sacrificed 4 weeks after surgery, and their tissues, namely the anterior prostate (AP), ventral prostate (VP), dorsolateral prostate (DLP), and bladder, were collected. The tissues were either fixed in 10% neutral buffered formalin or directly embedded into OCT. Formalin fixed tissues were then embedded into paraffin (FFPE) blocks and sectioned into 5 micron sections. FFPE tissues were stained with Masson's trichrome, Verhoeff's Van Gieson, and picrosirius red (PSR) to assess for collagen and elastin. Immunohistochemistry (IHC) staining was performed to detect BrdU to quantify cell proliferation within the prostate lobes. OCT blocks were sectioned at 10 micron thickness and assessed for senescence-associated β-galactosidase (SA-β-gal) activity.

RESULTS: Both groups of mice showed an increase in voiding frequency following steroid hormone implantation. The preliminary results from PSR analysis shows an increase of collagen deposition in the lower urinary tract for C57Bl6/NJ mice compared to C57Bl6/J mice.

CONCLUSIONS: Due to the genetic drift of the mouse colonies, we see differences in response to steroid hormones despite an increase in voiding dysfunction as measured by VSA. This suggests that sub-strains may model different etiologies of disease and should be carefully chosen.