The aryl hydrocarbon receptor agonist ITE reduces inflammation and urinary dysfunction in a mouse model of autoimmune prostatitis

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Abstract:
Prostate inflammation is linked to lower urinary tract dysfunction and is a key factor in chronic prostatitis / chronic pelvic pain syndrome. Autoimmunity was recently identified as a driver of prostate inflammation. Agonists of the aryl hydrocarbon receptor (AHR), a ligand-activated transcription factor, have been used to suppress autoimmunity in mouse models of colitis, rhinitis, and dermatitis, but whether AHR agonists suppress prostate autoimmunity has not been examined. Here, we test whether ITE (2-(1'H-indole-3'-carbonyl)-thiazole-4-carboxylic acid methyl ester), an AHR agonist, suppresses inflammation, allodynia, and urinary dysfunction in a mouse model of Experimental Autoimmune Prostatitis (EAP). C57BL/6J adult male mice were immunized with rat prostate antigen to induce Experimental Autoimmune Prostatitis (EAP) or TiterMax Gold® adjuvant (uninflamed control). Mice were also treated with ITE (10 mg/kg/day IP for 6 d) or DMSO (5 mg/kg/day) for 6d (vehicle). EAP heightened histological inflammation in the dorsal prostate, induced tactile allodynia, and increased the frequency of non-voiding bladder contractions. ITE significantly mitigated the actions of EAP. Using the Nanostring nCounter Inflammation Panel, we evaluated the impact of EAP and ITE on prostatic RNA abundance. EAP changed abundance of 40 inflammation-related RNAs, while ITE changed abundance of 28 inflammation-related RNAs. We identified a cluster of RNAs for which ITE protected against EAP-induced changes in the abundance of *H2-Ab1*, *S100a8*, and *S100a9*. ITE also increased the abundance of the AHR-responsive *Cyp1b1* RNA. These findings support the hypothesis that ITE activates the AHR and reduces autoimmune-mediated prostatitis in mice.

Keywords:
CP/CPPS, Experimental Autoimmune Prostatitis, AHR, ITE, Inflammation, Inflammasome, Therapeutic Strategies, Autoimmunity, Urology, Translational Animal Models