TNF is a Potential Therapeutic Target to Suppress Prostatic Inflammation and Benign Prostatic Hyperplasia in Autoimmune Disease

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Autoimmune (AI) diseases can affect many organs; however, the prostate has never been considered to be a target organ of these systemic inflammatory processes. These studies utilize medical record data, patient samples, and *in vivo* models to evaluate the impact of inflammation, as seen in AI diseases, on prostate tissue. Single-cell RNA-seq analysis is performed to detail the inflammatory milieu in human benign prostatic hyperplasia (BPH) tissues. Both human and mouse tissues are used to determine whether systemic targeting of inflammation limits prostatic inflammation and hyperplasia. Here, evaluation of 112,152 patient medical records indicate that BPH prevalence is significantly higher among patients with AI diseases. Furthermore, treating these patients with tumor necrosis factor (TNF)-antagonists significantly decreases BPH incidence. Single-cell RNA-seq and *in vitro* assays suggest that macrophage-derived TNF stimulates BPH-derived fibroblast proliferation. TNF blockade significantly reduces epithelial hyperplasia and ventral prostate volume from the Pb-PRL mouse model, which has prostate-specific expression of prolactin. Additionally, TNF blockade significantly reduces prostatic epithelial hyperplasia, NFκB activation, and macrophage-mediated inflammation within prostate tissues from an autoimmune mouse model (non-obese diabetic) and human patients. Together, these studies show that patients with AI diseases have a heightened susceptibility to BPH and that reducing inflammation with a therapeutic agent can suppress BPH.