Title: Claudin 1 is down-regulated in the aging prostate and associated with increased inflammation in BPH

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Background: Benign prostatic hyperplasia (BPH) is an age-related disease that is frequently associated with chronic prostatic inflammation. In our previous studies, we detected the presence of PSA protein in the stroma of BPH nodules and down-regulation of junction proteins E-cadherin and claudin 1. Transmission electron microscopy (TEM) imaging showed a decrease in tight junctions suggesting the luminal epithelial barrier in BPH tissues may be altered. Recent in vitro studies showed that stimulation of benign prostate epithelial cell lines with TGFβ1 induced a decrease in claudin 1 expression suggesting that inflammation might be associated with alterations in the prostate epithelial barrier. This study explored the potential associations between aging and loss of junction proteins and the presence of inflammatory cells in prostate tissue specimens from young healthy donors and aged BPH patients.

Method: Immunostaining of serial prostate sections from BPH patients and healthy young donors was performed for claudin 1, CD4, CD8, CD20 and CD68. H-Scores and the number of inflammatory cells were calculated for the same area in donor, normal adjacent prostate to BPH (NAP) and BPH specimens. Quantification and statistical correlation analyses were performed.

Results: Down-regulation of junction protein claudin 1 was associated with increasing age and inflammation in NAP and BPH compared to young healthy donor prostate.

Conclusions: These findings suggest that aging is associated with down-regulation of claudin 1 and claudin 1 is further decreased in BPH. Claudin 1 down-regulation was associated with increased infiltration of inflammatory cells in both NAP and BPH tissues. Claudin down-regulation in the aging prostate could contribute to increased prostatic inflammation, subsequently contributing to BPH pathogenesis.