A multiscale survey of inflammatory diseases and prostate oncophenotypes.

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Background: Prostate cancer (PCa) is the most common cancer detected in men (181,000 annual cases), and nearly 26,000 American men die each year due to PCa and related complications. Reports have shown that PCa is more aggressive when its comorbid with inflammatory diseases. However, the correlations and risks attributed to inflammatory diseases of the abdominal cavity and oncophenotypes are not known. *Methods*: To investigate how inflammatory pathways and PCa genes induce aggressive oncophenotypes in the setting of PCa, we have compiled a multiscale survey that includes data from surgical observations, inflammatory phenotypes, clinical registries, biomarkers and mouse models. We applied an integrative informatics approach with experimental validation to understand the associations between inflammatory diseases (e.g., Crohn's disease, ulcerative colitis, collagenous colitis, indeterminate colitis, ischemic colitis, diverticulitis, hernia, etc.) and PCa. *Results*: We found distinct patterns of shared molecular features---gene sets, pathways, and networks---and comorbidities across inflammatory disease and PCa. For example, we found that diverticulitis tend to increase inflammation in the abdominal cavity and could potentially lead to aggressive prostate oncophenotypes. To test abdominal inflammation and PCa correlation, we induced inflammation in a mouse model of hiatus hernia, which resulted in an increase in the expression of the combined markers of inflammation and PCa (*TGFB, TNFA, and IL6*). Evaluation of pathology stage, Gleason scores and physical attributes of previous inflammation observed during robotic prostatectomy surgery also reveals trend towards aggressive tumor characteristics with an increase in inflammation. Gene-set overlap analyses showed that several inflammatory disease and prostate cancer genes share genetic modules. *Conclusion*: Collectively, our findings provide the first set of computational, experimental and clinical evidence to recommend clinicians to evaluate the impact of inflammatory disease induced oncophenotypes in patients with PCa. Given that 1.3 million patients undergo prostate-specific antigen (PSA)-triggered invasive trans-rectal biopsy, the present findings in combination with PSA could facilitate the identification patient subset with aggressive cancer. Stratifying patients at risk for prostate cancer who are undergoing surgical interventions of abdominal cavity for inflammation diseases could also evaluate other non-surgical or therapeutic strategies.

Conflict of Interest: None