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IL-17-MMP7-EMT AXIS AS POTENTIAL DRUGGABLE TARGET IN THE PREVENTION AND TREATMENT OF PROSTATE CANCER

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Th17 cells are a subset of T helper cells secreting interleukin-17 (IL-17A and IL-17F). We have systematically investigated the role of IL-17 in prostate cancer. We found that IL-17 receptor C (IL-17RC) expression was up-regulated in human prostatic intraepithelial neoplasia (PIN), hormone naïve prostate cancer, and castration-resistant prostate cancer. Using an Il-17rc;Pten (Phosphatase and tensin homolog) double knockout mouse model, we found that IL-17 promoted development of hormone-naïve and castration-resistant prostate cancer through multiple mechanisms, including: 1) directly stimulating expression of cytokines, chemokines, and growth factors; 2) directly inducing inflammatory cell infiltration; 3) increasing the ratio of immunosuppressive immune cells; 4) increasing angiogenesis; 5) enhancing cellular proliferation; and 6) inhibiting cellular apoptosis. Using an Mmp7;Pten double knockout mouse model, we found that MMP7 promoted prostate adenocarcinoma through induction of epithelial-to-mesenchymal transition (EMT). IL-17 induced MMP7 and EMT in human prostate cancer cell lines, while siRNA knockdown of MMP7 inhibited IL-17-induced EMT. Selective inhibitor of MMP7, inhibitor of Th17 cell differentiation, and anti-IL-17A neutralizing antibodies were able to partially inhibit prostate cancer formation in the Pten knockout mice. These findings demonstrate that IL-17-MMP7-EMT axis plays an important role in prostate cancer development, indicating IL-17-MMP7-EMT axis as a potential target for developing new strategies in the prevention and treatment of prostate cancer.

BIOGRAPHY

Zongbing You received his MD at the age of 23 years and PhD at the age of 28 years from West China University of Medical Sciences, Chengdu, China. He is a tenured Associate Professor and Vice Chair for Research as well as Director of the Two-Year Research Master's Degree Program in the Department of Structural and Cellular Biology at Tulane University School of Medicine, New Orleans, Louisiana, USA. He has published 80 publications and edited a professional book. His research interest is in inflammation and prostate cancer.

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