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CXCL-TYPE CHEMOKINES–INDUCED FIBROSIS IN THE LOWER URINARY TRACT
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Introduction: Recent studies from our group suggest that extracellular matrix (ECM)
deposition and fibrosis characterize the peri–urethral prostate tissues of some men
suffering from Lower Urinary Tract Symptoms (LUTS). Fibrosis can generally be regarded
as an errant wound–healing process in response to chronic inflammation, and studies
have shown that the aging prostate tissue microenvironment is rich with inflammatory
cells and proteins. However, it is unclear whether these same inflammatory proteins,
particularly CXC–type chemokines, can mediate myofibroblast phenoconversion and the
ECM deposition necessary for the development of prostatic tissue fibrosis.

Methods: Peri–urethral prostate tissues were disaggregated and subjected to FACS for
expression of CD45 and collagen I. Primary stromal fibroblasts were cultured from
explanted human peri–urethral prostatic tissues. N1 immortalized or primary prostate
stromal fibroblasts were treated in serum–free defined media with TGF–β, CXCL5,
CXCL8, or CXCL12 and evaluated using immunofluorescence or qRT–PCR for αSMA,
collagen I, collagen III, vimentin, calponin, and tenascin protein and transcript expression,
and by gel contraction assays for functional myofibroblast phenoconversion. The
specificity of these responses to treatment with CXCL12 was assessed using a small
molecule inhibitor, AMD3100, of the CXCL12 receptor, CXCR4.

Results: The results of these studies showed that peri–urethral prostate tissues
comprised both myofibroblastic and fibroblastic cell types, but that CD45+/collagen I+
fibrocytic cells were identified exclusively in peri–urethral tissues from men suffering from
LUTS. Both N1 immortalized and primary prostate stromal fibroblasts exhibited
complete and functional myofibroblast phenoconversion and were induced to express
collagen I, collagen III and αSMA gene transcripts and proteins in response to treatment
with CXC–type chemokines, even in the absence of exogenous TGF–β1.

Conclusions: These findings suggest that CXC–type chemokines, particularly CXCL12,
can efficiently and completely mediate myofibroblast phenoconversion and may thereby
promote fibrotic changes in prostate tissue architecture associated with the development
and progression of male lower urinary tract dysfunction.

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(JAM)