Nature Reviews Urology **12**, 652 (2015); published online 10 November 2015; doi:10.1038/nrurol.2015.273

PROSTATE CANCER

Dysregulated stress-related signalling pathways associated with lethality of prostate cancer

Findings from a new study indicate that dysregulation of stress-related signalling pathways—in particular the adrenergic and glucocorticoid pathways—is associated with prostate cancer lethality.

Previous studies have indicated that stress-induced neurotransmitters and hormones might alter tumour microenvironment and influence tumour progression. Lu and co-workers aimed to test the hypothesis that mRNA expression of genes within five major stress-related signalling pathways are differentially expressed in the tumour tissue of men with lethal prostate cancer and those with non-lethal prostate cancer.

Lu and colleagues measured mRNA expression of 51 genes involved in five major stress-related signalling pathways (the adrenergic, dopaminergic, glucocorticoid, muscarinic and serotoninergic pathways) in tumour tissue ($n = 404$) and normal tissue ($n = 202$) from patients with prostate cancer. They looked at differences in pathway expression in relation to the lethality of prostate cancer as the primary outcome, and in relation to biomarkers as secondary outcomes.

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The researchers found significant associations between lethal prostate cancer and differential signalling in prostate tumour tissue for four pathways—the adrenergic, glucocorticoid, serotoninergic and muscarinic pathways. After controlling for Gleason score and tumour stage, the findings for the glucocorticoid and serotoninergic pathways remained statistically significant. The team did not find differential expression of the pathways in the adjacent normal tissue of lethal prostate cancer compared with that of nonlethal prostate cancer. They found that the glucocorticoid and adrenergic pathways were associated with cell proliferation and that the glucocorticoid pathway was also associated with angiogenesis and perineural invasion.

“...this is, to the best of our knowledge, the first large study on men with prostate cancer to comprehensively investigate the association between stress-related signalling pathways and prostate cancer progression at the transcription level,” say the authors. “Future research is needed to confirm these associations, understand when alteration of these pathways occurs, and determine whether intervention through these signaling pathways could be effective for intervention.”

Rebecca Kelsey

Original article Lu, D. *et al.* Stress-related signaling pathways in lethal and non-lethal prostate cancer. *Clin. Cancer Res.* doi:10.1158/1078-0432.CCR-15-0101