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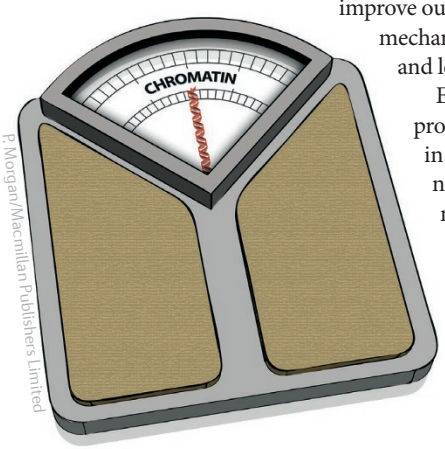
PROSTATE CANCER

A weighty issue: changes in chromatin regulation



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Differences between the expression of chromatin-related genes in prostate cancer tissue from very-overweight or obese men and cancer tissue from men with a normal BMI have been identified. These observations could improve our understanding of the mechanistic link between obesity and lethal prostate cancer.

Ericka Ebot and colleagues profiled gene expression in tumour and adjacent nondiseased tissue from men diagnosed with prostate cancer. The BMI of these participants was prospectively collected immediately before cancer diagnosis; healthy weight was defined as BMI 18.5–<25 kg/m^2, overweight as 25–<27.5 kg/m^2, and very overweight or obese as ≥27.5 kg/m^2.

Gene-set-enrichment analysis (GSEA) revealed 15 upregulated and two downregulated gene sets between tissue from very-overweight or obese men and men of healthy weight; however, these gene sets were not differentially regulated in nondiseased tissue, suggesting these changes are tumour-specific. Of the 15 upregulated gene sets, five contained genes involved in chromatin modification and remodelling.

The investigators created a metagene score to categorize the chromatin gene set network, based on the expression of the 35 genes comprising the GSEA leading-edge subset — all of these genes were upregulated in the ≥27.5 kg/m^2 group. This score was significantly positively associated with Gleason grade and prediagnosis BMI in tumour tissue, but not adjacent nondiseased tissue. Furthermore, this score was positively associated with risk of lethal prostate cancer.

Ebot told *Nature Reviews Urology* "Our findings provide biological support for obesity as a driver of aggressive prostate cancer, and suggest that chromatin regulation is an important mechanism to explore further. Future studies are aimed at validating these findings and identifying obesity-related chromatin biomarkers for high-risk disease." She continued: "the development and validation of an obesity-associated chromatin signature in prostate tissue could provide biomarkers for future clinical testing. Furthermore, an improved understanding of epigenetic events in prostate cancer progression might uncover novel therapeutic targets for treatment in all men with this disease, regardless of obesity status."

Louise Stone

ORIGINAL ARTICLE Ebot, E. M. *et al.* Gene expression profiling of prostate tissue identifies chromatin regulation as a potential link between obesity and lethal prostate cancer. *Cancer* http://dx.doi.org/10.1002/cncr.30831 (2017)