

 PROSTATE CANCER

Tumour genomes are highly plastic

“
Driver
aberrations
were found in
cancer-related
genes”

Many changes in somatic copy-number alterations (SCNAs) containing potential driver genes occur during the progression of metastatic prostate cancer — particularly in focal amplifications — according to new research published in *Nature Communications*. The observation that tumour genomes have high plasticity has considerable consequences for patient treatment and also the testing of new androgen deprivation therapies (ADTs).

Peter Ulz and co-workers used plasma-Seq¹⁰ — a technique that uses whole-genome sequencing of DNA from plasma at a shallow sequencing depth to identify SCNAs from circulating tumour DNA (ctDNA) — to screen a panel of 95 plasma samples from 43 patients with metastasized prostate cancer. They observed SCNAs in 77.8% of these samples, which compared with a prevalence of 77.5% in samples from The Cancer Genome Atlas. Driver aberrations were found in cancer-related genes, including driver gene fusions in *TMPRSS2:ERG*, driver focal deletions in *PTEN*, *RYBP* and *SHQ1*, and driver amplifications in *AR* and *MYC*.

Analysis of serial blood samples from 15 men showed that six of them had changes in the focal SCNA status of their ctDNA and the mean time between these focal alterations was 26.4 weeks. Some patients also experienced an increase in neuron-specific enolase that was accompanied by changing clonal patterns and low serum PSA concentrations, which could indicate transdifferentiation from adenocarcinoma to neuroendocrine prostate cancer.

The high tumour plasticity observed in this study has substantial implications for clinical trials and testing of novel ADTs. These data also suggest that prostate cancer can rapidly adapt to selection pressure and that use of plasma-Seq¹⁰ (which is a low-cost technique with a rapid <48 h turnaround time) could be practical to monitor these changes and aid in treatment selection.

Louise Stone

ORIGINAL ARTICLE Ulz, P. *et al.* Whole-genome plasma sequencing reveals focal amplifications as a driving force in metastatic prostate cancer. *Nat. Commun.* <http://dx.doi.org/10.1038/ncomms12008> (2016)