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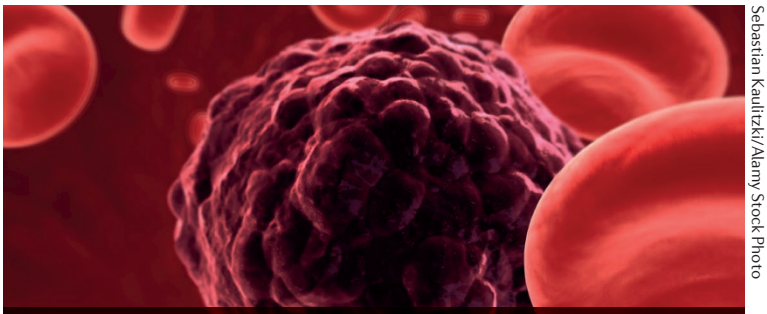

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PROSTATE CANCER

CTC phenotype informs treatment type

Results of a study published in *Cancer Research* show that analysing the phenotypic heterogeneity of circulating tumour cells (CTCs) can inform the clinical decision of which type of treatment to give men with metastatic castration-resistant prostate cancer (mCRPC) and improve outcomes for these patients.

Investigators collected a total of 319 blood samples from 179 patients before starting or whilst receiving treatment for mCRPC (221 before therapy and 97 during therapy); these samples were split into two groups. All 319 samples formed the contributing cohort, which was analysed for automated feature extraction of characteristics including protein biomarker expression and digital pathology features. A subset of 145 pretherapy samples from the contributing cohort, from men before starting or whilst receiving second-line or later-line therapy, were used for the clinical association cohort (86 from men prescribed an androgen receptor signalling inhibitor (ARSI) and 59 from men prescribed a taxane).

CTC phenotypic heterogeneity was analysed using the Shannon index, which can measure phenotypically defined CTC subtypes. These subtypes were created using unsupervised clustering of single-cell features from 9,225 CTCs identified from the contributing cohort. Overall 15 CTC phenotypic subtypes were identified. Each patient sample was then assessed for subtype diversity.

Median overall survival estimates remained constant with respect to Shannon index for patients receiving a taxane. However, for patients prescribed an ARSI, a low Shannon index (low CTC heterogeneity) correlated with increased survival estimates compared with taxane therapy, whereas patients with a high Shannon index (high CTC heterogeneity) receiving an ARSI had reduced survival estimates relative to those receiving a taxane.

A significant difference in median overall survival between men with a high or low Shannon index receiving an ARSI was observed (8.8 months versus 28.1 months, $P = 0.0015$); such a difference was not observed for men prescribed a taxane. On multivariate analysis, the interaction between increased Shannon index and reduced estimated overall survival for men on an ARSI relative to men receiving a taxane remained significant. Furthermore, an alternative measure of intrapatient phenotypic heterogeneity, the pleomorphic index, showed similar results.

These results show that intrapatient CTC phenotypic heterogeneity that is present before therapy initiation can influence survival outcomes in a treatment-dependent manner. Thus, quantifying CTC heterogeneity before starting treatment can inform therapy decisions and improve outcomes for men with mCRPC.

Louise Stone

> “low Shannon index (low CTC heterogeneity) correlated with increased survival estimates”

ORIGINAL ARTICLE Scher, H. I. *et al.* Phenotypic heterogeneity of circulating tumor cells informs clinical decisions between AR signaling inhibitors and taxanes in metastatic prostate cancer. *Cancer Res.* http://dx.doi.org/10.1158/0008-5472.CAN-17-1353 (2017)