PROSTATE CANCER INTEGRATED TEST PREDICTS OUTCOME

A novel 100-loci DNA signature that combines data on genomic instability and intratumoral hypoxia can improve prognostic accuracy in patients with localized prostate cancer, according to new research published in *The Lancet Oncology*.

Allocation of patients with low-risk or intermediate-risk prostate cancer to optimum treatment groups to avoid overtreatment, but also early clinical relapse, remains challenging. In a new retrospective cohort study, Emilie Lalonde, Adrian Ishkanian and colleagues developed a novel approach to stratify patients for risk of 5-year biochemical recurrence independent of prior first-line treatment.

First, based on copy number alterations, the researchers identified four distinct genomic subtypes that had significantly different prognoses. Under the hypothesis that the percentage of genomic alteration (genomic instability) in itself might be prognostic, the team demonstrated that every 1% increase in alteration resulted in a 5–8% decrease in 5-year biochemical recurrence-free survival. In addition, genomic instability was prognostic for relapse in patients who underwent image-guided radiotherapy (HR 4.5; 95% CI 2.1–9.8) or radical prostatectomy (HR 4.0; 95% CI 1.6–9.7).

Next, the researchers examined the influence of intratumoral hypoxia and observed that the prognostic accuracy of genomic instability was increased when incorporating hypoxia values.

Finally, the team developed a genomic signature to integrate the interactions between the genes responsible for the discovered prognostic properties. Their analysis revealed a 100-loci DNA signature involving 276 genes, whose ability to predict biochemical failure was validated in two independent patient cohorts. In low-risk and intermediate-risk patients who underwent radical prostatectomy, the biopsy-based model effectively identified those men who were most likely to fail treatment within 18 months (HR 2.9; 95% CI 1.4–6.0). Notably, the new test performed better than 23 previously published RNA signatures.

The team envision their predictive model to be used for improved enrolment of patients into clinical trials of optimized therapies or active surveillance.

Clemens Thoma

Original article Lalonde, E. *et al.* Tumour genomic and microenvironmental heterogeneity for integrated prediction of 5-year biochemical recurrence of prostate cancer: a retrospective cohort study. *Lancet Oncol.* doi:10.1016/S1470-2045(14)71021-6