PATHOLOGY

Prostate cancer—personalized response prediction

Prostate cancer is the most commonly diagnosed malignancy among men. Aside from measurement of clinical variables, no tests can reliably identify disease progression in these patients. Donovan and colleagues have developed a patient-specific, biology-driven tool to predict the outcome of patients with prostate cancer at diagnosis. "To address this issue our approach has been to generate predictive, tumor-specific tools using technological advances in morphometry and quantitative immunofluorescence", state the investigators, in their paper.

The researchers evaluated paraffin-embedded tissue obtained by needle biopsy from 1,027 men with cT1c–T3 prostate cancer who underwent prostatectomy and were followed up for a median of 8 years. Patients were divided into a training group ($n = 686$) and a validation group ($n = 341$). Tumor slides were stained with hematoxylin and eosin, and Gleason scores and grades were determined. Clinical data were integrated with biopsy quantitative biometric features and multivariate models were constructed to predict disease progression.

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In the training group, three clinical and three biopsy tissue characteristics predicted clinical progression within 8 years after prostatectomy, with a sensitivity of 78%, a specificity of 69%, a C index of 0.74 and a hazard ratio of 5.12. These findings were verified in the independent validation cohort, which resulted in a sensitivity of 76%, a specificity of 64%, a C index of 0.73 and a hazard ratio of 3.47. Moreover, increased androgen receptor levels in tumor biopsy samples were significantly associated with resistance to therapy.

The researchers found that morphometry accurately classified Gleason score 3 tumors and that, in combination with biomarker data, this technique increased the accuracy of the parameters currently used to predict outcome at diagnosis. Moreover, as androgen receptor levels in biopsy samples were predictive of the response to therapy following disease recurrence, future treatment decisions might be formulated based on these results. "We anticipate that the biological basis for the high risk classification, including transition to a Gleason 4 pattern and high androgen receptor [expression], will be used as part of the therapeutic process", conclude the researchers.

Vessela Vassileva

Original article Donovan, M. J. *et al.* Personalized prediction of tumor response and cancer progression on prostate needle biopsy. *J. Urol.* **182**, 125–132 (2009).