GENETICS

First prognostic signature for adjuvant lung cancer therapy

The introduction of adjuvant cisplatin-based chemotherapy (ACT) to the treatment options for patients with resected non-small-cell lung cancer (NSCLC) has improved survival. 5-year survival was improved by 4–15%, but no survival effects have been observed in patients with early-stage I disease. Indeed, it has been reported that patients with stage IA disease might be detrimentally affected by treatment with ACT.

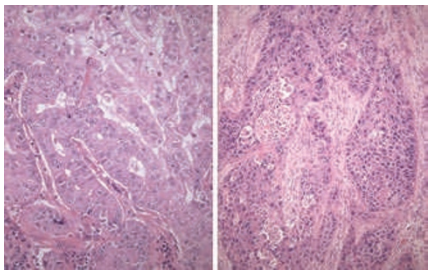
"Currently there is a need for prognostic and predictive molecular biomarkers, independent of tumor stage, to select early-stage NSCLC patients to be treated by ACT," explained Ming-Sound Tsao. Tsao led a group of researchers who addressed this problem using gene-expression profiling to assess mRNA from 133 frozen samples from the randomized JBR.10 trial that compared ACT with observation.

A 15-gene signature was obtained from the 62 samples of patients treated with surgery alone then, as Tsao explains, "a new method based on maximum R^2 analysis was used to identify a minimum gene set that can clearly distinguish the poor from good prognosis patients."

The identified 15-gene signature was validated using four independent datasets and by quantitative reverse-transcription PCR. This revealed that the signature was an independent prognostic factor.

Other signatures have been reported for NSCLC, the difference in this study was highlighted by Tsao; "the signature was then tested in the microarray data of 71 JBR.10 patients who received ACT for its ability to predict benefit from ACT." JBR.10 has snap-frozen tumor samples available for gene-expression analysis from both treated and observation patients, and Tsao and his team have taken advantage of this opportunity.

The signature also classified the 71 chemotherapy-treated patients into low-risk and high-risk groups; ACT prolonged survival in the high-risk patients but was not beneficial, and potentially even detrimental, in low-risk patients.



Histology of non-small-cell lung cancer. Left panel, adeno-carcinoma; right panel, squamous cell carcinoma. Image courtesy of M. S. Tsao.

Future plans for these data include "the development of a small-gene-set assay that can be performed more easily in clinical diagnostic laboratories and prospective validation of the signature in future early-stage NSCLC adjuvant chemotherapy trials," explained Tsao.

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