## GENETICS

Four-gene signature predicts survival in NSCLC

Non-small-cell lung cancer (NSCLC) is the most common type of lung cancer. Surgery is the treatment of choice for early-stage disease; however, metastasis is a major cause of death in NSCLC patients. The management of NSCLC could be improved if patients at risk for developing metastasis or recurrence could be identified. A critical factor in metastasis is the migration and invasive abilities of cancer cells. Researchers have investigated gene signatures to understand the invasive ability of cancer cells and to predict disease outcome. In an attempt to understand metastasis Hsu and colleagues identified invasion-associated genes from nine lung cancer cell lines in the NCI-60 gene expression data set (A549/ATCC, NCI-H460, NCI-H23, NCI-H322M, EKVX, NCI-H226, NCI-H522, HOP-62 and HOP-92) and validated the results using three independent cohorts.

The investigators began by conducting an invasion assay to distinguish the invasive abilities of NCI-60 lung cancer cell lines and then used NCI-60 microarray databases to identify invasion-associated genes, differentiating between high and low invasion cell lines. Using microarray data from the Duke lung cancer cohort (GSE 3141, $n = 111$) they identified invasion-associated genes with good survival potential. These findings were then confirmed by conducting quantitative PCR assays on frozen sections of lung cancer tissue from a group of 69 patients from Taiwan and from two Western public cohorts consisting of 257 and 186 patients from four institutions
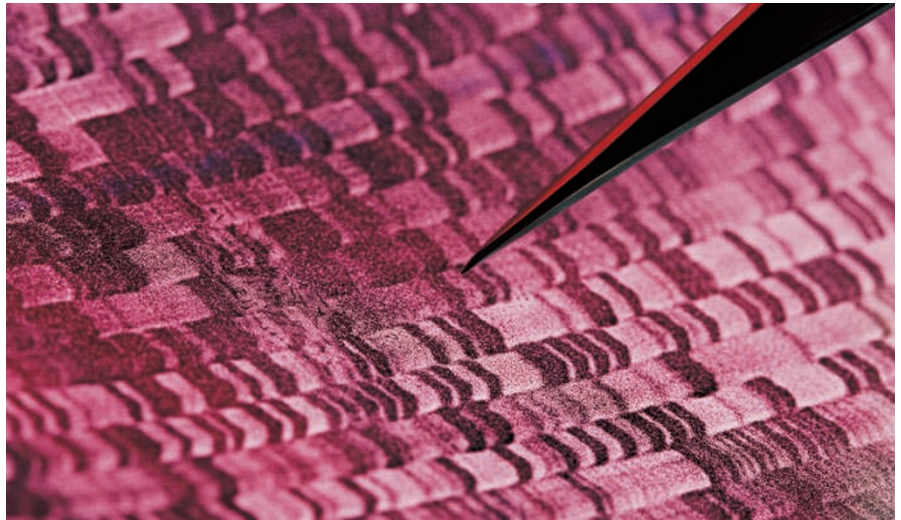
in the US. Cox proportional hazard regression analysis was used to determine the association between survival and gene expression. The Kaplan–Meier method was used to estimate overall survival for patients in each group.

The authors found that the invasion-associated four-gene signature (ANKRD49, LPHN1, RABAC1 and EGLN2) had significant predictive value in the three cohorts ($P = 0.0184$, 0.002 and 0.033) and was an independent prognostic factor for survival ($P = 0.028$, 0.014 and 0.033; hazard ratio 2.354, 1.480 and 1.670), independent of other variates including age, gender and disease stage. As predicted by the four-gene signature, patients with the high-risk gene signature had reduced median overall survival compared with patients with the low-risk gene signature.

The authors concluded that "an invasion associated gene signature derived from NCI-60 lung cancer cell lines by our in silico microarray approach had good survival prediction power in NSCLC patients." They added "For clinical applications, the smaller number of genes in the signature may have the greater potential of translating into practical methods of lung cancer patient risk stratification and developing personalized therapy." The four invasion-associated genes in the signature could, therefore, be potential targets for lung cancer therapy.

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Original article Hsu, Y. *et al.* A four-gene signature from NCI-60 cell line for survival prediction in non-small cell lung cancer. *Clin. Cancer Res.* **15**, 7309–7315 (2009)