

Prognostic gene signatures for lung adenocarcinoma using digital multiplexed gene expression in formalin-fixed paraffin embedded tissue

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BACKGROUND: The outcome after resection of non-small-cell lung cancer (NSCLC) patients are poor, even in the early stage, there still has 35-50% recurrence rates. Current staging methods are not inadequate for predicting the outcome of NSCLC patients.

HYPOTHESIS: We aimed to develop a more reliable gene signature that improves the risk prediction compared with the traditional staging.

METHODS: 396 lung adenocarcinoma specimens were obtained for this study, of whom 78 frozen specimens (cohort1) and 223 FFPE specimens (cohort2) were from Shanghai Cancer Center, Fudan University and 85 FFPE specimens (independent cohort) were from Shanghai Pulmonary Hospital. The RNA was extracted from cohort1 and used in the microarray gene expression analysis to derive prognostic associated genes. The digital multiplexed technology (Nanostring) was then used to determine the expression of these genes in FFPE-derived RNA from cohort2. For validation, we used the random patients from the independent cohort.

RESULTS: Through microarray assay, the top 18 survival and 19 metastasis associated gene were chosen to digital multiplexed gene expression analysis using FFPE-derived RNA from cohort2. Four genes that correlated with the survival were then identified by risk scores. Kaplan-Meier analysis showed that patients of high risk scores had longer OS and DFS compared with patients of low risk scores in the cohort2. The four-gene signature was an independent predictor of OS and DFS. We validated the four-gene model in the independent cohort.