Gene profiling of clinical routine biopsies and prediction of survival in non-small cell lung cancer

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RATIONALE: Global gene expression analysis provides a comprehensive molecular characterization of non-small cell lung cancer (NSCLC). OBJECTIVES: To evaluate the feasibility of integrating expression profiling into routine clinical work-up by including both surgical and minute bronchoscopic biopsies and to develop a robust prognostic gene expression signature. METHODS: Tissue samples from 41 chemotherapy-naive patients with NSCLC and 15 control patients with inflammatory lung diseases were obtained during routine clinical work-up and gene expression profiles were gained using an oligonucleotide array platform (NovaChip; 34'207 transcripts). Gene expression signatures were analyzed for correlation with histological and clinical parameters and validated on independent published data sets and immunohistochemistry. MEASUREMENTS AND MAIN RESULTS: Diagnostic signatures for adenocarcinoma and squamous cell carcinoma reached a sensitivity of 80%/80% and a specificity of 83%/94%, respectively, dependent on the proportion of tumor cells. Sixty-seven of the 100 most discriminating genes were validated with independent observations from the literature. A 13-gene metagene refined on four external data sets was built and validated on an independent data set. The metagene was a strong predictor of survival in our data set (hazard ratio = 7.7, 95% CI [2.8-21.2]) and in the independent data set (hazard ratio = 1.6, 95% CI [1.2-2.2]) and in both cases independent of the International Union against Cancer staging. Vascular endothelial growth factor-beta, one of the key prognostic genes, was further validated by immunohistochemistry on 508 independent tumor samples. CONCLUSIONS: Integration of functional genomics from small bronchoscopic biopsies allows molecular tumor classification and prediction of survival in NSCLC and might become a powerful adjunct for the daily clinical practice.