Molecular characterization of lung cancer by mRNA expression profiling

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Lung cancer remains the leading cause of cancer death in industrialized countries. The current lung cancer classification is based on clinicopathological features. Briefly, first of all, they are classified as small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC). Neuroendocrine features, defined by microscopic morphology and immunohistochemistry, are hallmarks of the high-grade SCLC and large cell neuroendocrine tumors and of intermediate/ low-grade carcinoid tumors. NSCLC is histopathologically and clinically distinct from SCLC, and is further subcategorized as adenocarcinoma (about 35% in Korea), squamous cell carcinoma (about 35% in Korea), and large cell carcinoma (about 10% in Korea) and others. Most patients with non-small cell lung cancer (NSCLC) present with advanced disease, and despite recent advances in multi-modality therapy, the overall 10-year survival rate remains a dismal 8-10%. However, a significant minority of patients (~25-30%) with NSCLC have locally advanced disease (stage I and II), and receive surgical intervention alone. Although 35-50% of patients with stage I disease will relapse within 5 years, it is not currently possible to identify specific high-risk patients. Currently, the only effective prognostic indicator for NSCLC in clinical use is surgical-pathological staging. However, staging system cannot identify specific high-risk patients within a certain stage, there is a need to identify patients at high risk for recurrent or metastatic disease. Preoperative variables that affect survival of patients with NSCLC have been identified. Tumor size, vascular invasion, poor differentiation, high tumor-proliferative index and several genetic alterations, including K-*ras* and p53 mutations, have prognostic significance. Multiple independently assessed genes or gene products have also been investigated to better predict patient prognosis in lung cancer. Technologies that simultaneously analyze the expression of thousands of genes can be used to correlate gene-expression patterns with numerous clinical parameters including patient outcome to better predict tumor behavior in individual patients. Here are the examples of clinical parameters, which we have tried to correlate with the gene-expression patterns.

1. pathological subtype of lung cancer
2. lymph node metastasis
3. prognosis within the stage, and within the same pathologic subtype
4. sexual difference
5. smoking history
6. pattern of recurrence, i.e., local vs distant failure of the treatment

Technically, we have used total RNA from microdissected tumor cells from the fresh-frozen tumor tissues of 110 curatively-resected NSCLC Korean patients at Samsung Medical Center, cDNA amplification and 10k cDNA microarray slides. The data have been analyzed by hierarchical clustering, permutation t-test. Logistic regression and Cox regression. Although the project is still on-going, current results permits hopeful expectation of the usefulness of the gene-expression patterns in clinical practice.