Metabolomic Profiling for the Early Detection of Lung Cancer

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Background:
Currently, the five-year survival rate of lung cancer patients is very low, largely attributed to newly diagnosed patients presenting with locally advanced or metastatic disease. The lung cancer five-year survival rate (18.6%) is lower than many other leading cancer sites, such as colorectal (64.5%), breast (89.6%) and prostate (98.2%). The five-year survival rate for lung cancer is 56% for cases detected when the disease is still localized (within the lungs). However, only 16% of lung cancer cases are diagnosed at an early stage. For distant tumors (spread to other organs) the five-year survival rate is only 5%. More than 50% of lung cancer cases die within one year of being diagnosed. Accordingly, early diagnosis is key to the successful treatment, management and care of lung cancer.

Methods:
Metabolomic techniques were used to discover and validate plasma biomarkers for the diagnosis of early-stage non-small cell lung cancer (NSCLC). Plasma samples from 599 patients with biopsy-confirmed NSCLC along with age and sex-matched plasma samples from 214 controls were analyzed. A fully quantitative targeted mass spectrometry analysis (targeting 142 metabolites) was performed. The sample set was split into a discovery set and validation set. Metabolite concentrations, clinical data, and smoking history were used to determine optimal sets of biomarkers and optimal regression models for identifying different stages of NSCLC using the discovery sets. The same biomarkers and regression models were used and assessed on the validation models.

Results:
Univariate and multivariate statistical analysis identified β-hydroxybutyric acid, LysoPC 20:3, PC ae C40:6, citric acid, and fumaric acid as being significantly different between healthy controls and early stage (I/II) NSCLC. Predictive models with AUC > 0.8 were developed and validated using these metabolites and other clinical data for detecting different stages of NSCLC.

Conclusions:
This study has identified and validated a simple, high-performing, metabolite-based test for detecting early stage (I/II) NSCLC patients in plasma. Such an observation will enable a blood-based routine screening test for patients at the highest risk for lung cancer that is cost-effective, accurate and reliable.