Aim: Lung cancer (LC) screening using low-dose CT demonstrated a 20% reduction in lung cancer mortality in heavy smokers. However, this strategy has several limitations including high false-positive rates, over-diagnosis, cost and the potential harm associated with radiation exposure. The aim was to identify differentially-expressed miRNAs in the serum of LC patients that might be a clinically-useful tool for LC early detection.

Methods: miRNA expression profile analysis using TaqMan OpenArray Human microRNA panel was performed in 70 serum samples obtained at lung tumor resection and 22 non-cancer subjects (NC). The discovery set included 86% adenocarcinoma (AC) and 14% squamous cell carcinoma (SCC). Selected serum miRNAs were validated by quantitative PCR in an independent set of serum samples from LC patients (n = 85) and NC (n = 23). The test set included 65% of patients with lung AC and 35% with lung SCC. In both sets, most patients were stage I (discovery, 57%; test, 67%) and LC patients and NC were age and gender matched.

Results: By class-comparison analysis, 55 miRNAs were found significantly up-regulated and 34 down-regulated in the serum from LC patients versus NC (adjusted p-value <0.001). We selected 4 miRNAs (miR-193b, miR-301, miR-141 and miR-200b) for validation of their diagnostic value based on the following criteria: overexpressed both in lung tumors and serum from LC patients and not up-regulated in blood cells. In the discovery set, the receiver operating curve derived from the combination of these miRNAs yielded an area under the curve (AUC) of 0.952 (95% CI 0.888–1.016, p < 0.001). In the test set, this miRNA signature exhibited an AUC of 0.965 (95% CI 0.912–1.019, p < 0.001) for AC and 0.961 (95% CI 0.915–1.007, p < 0.001) for SCC. The performance of the miRNA signature remained unchanged when the analysis was restricted to stage I tumors. A pathway analysis based on the predicted targeted genes revealed that these 4 miRNAs were associated with ErbB, MAPK, p53, PI3K-AKT, NSCLC and mTOR signaling pathways.

Conclusions: We identified a serum 4-miRNA signature that discriminated with high accuracy LC patients from NC. Although this miRNA signature was validated in an independent cohort, further prospective validation in warranted in additional cohorts of subjects at high risk of LC.

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