Combining Metabolomics and Liquid Biopsy to Identify Diagnostic and Prognostic Biomarkers in Patients with Non-Small Cell Lung Cancer

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Lung cancer is considered the deadliest form of cancer, primarily due to late diagnosis and lack of early detection methods, with non-small cell lung cancer (NSCLC) representing over 85% of all lung cancer cases and is generally associated with poor prognosis in advanced stages. In this study, we investigated changes in circulating metabolite levels in NSCLC patients versus healthy controls, and between NSCLC patients with different disease stages (ongoing versus progressive disease). Sixteen NSCLC patients were enrolled in the study (eight ongoing and eight PD) and five healthy controls. Plasma metabolite levels were assessed using untargeted metabolomics employing UHPLC-tims-Q-ToF-MS in both electrospray ionization modes. A clear discrimination between the different groups was achieved using multivariate chemometrics techniques and univariate statistical analysis. The study revealed five elevated and seven reduced metabolites in patients versus healthy controls, while in relapsed patients, one metabolite was upregulated and five metabolites were downregulated. The primary discriminatory and differential metabolites included D-lactic acid, D-glucose, L-arginine, L-cystine, L-tryptophan, Glutamine, Creatine, Betaine, Glycerophosphocholine, Indoleacrylic acid, 5-acetylamino-6-formylamino-3-methyluracil, 2,6 dimethylheptanoyl carnitine, 6-keto-decanoylcarnitine, Oleic acid and Choline. These results suggest disruptions in the metabolic pathways of glucose, amino acids, and phospholipids in patients with lung cancer. In conclusion, metabolomics identified distinct metabolic profiles in patients with NSCLC, offering potential diagnostic and prognostic biomarkers.

Keywords: biomarkers; lung cancer; metabolomics; liquid biopsy; mass spectrometry