Pre- and Post-Surgery Metabolomic Profiles in Early-Stage NSCLC Patients

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Background: Finding biomarkers to detect cancer at its early stage is of importance. Since metabolic reprogramming is a hallmark of cancer, oncometabolite is thus a promising target. Progress in cancer metabolomics opens the door for extensive scale screening of cancer-specific metabolites that could be future applied for subclinical stage detection and novel therapeutic targets.

Methods: Seventy paired pre- and postoperative plasma samples of early-stage non-small cell lung cancer (NSCLC) patients who had completed curative surgery during 2015-2018 with ≥ 3 months of disease-free were retrieved. Demographic and Clinical data were collected. All samples were subjected to targeted metabolomics analysis using AbsoluteIDQ® p180 Kit combined with Flow injection analysis and Liquid chromatography tandem mass spectrometry. Multivariate analysis including Principal Components Analysis (PCA) and Orthogonal Partial Least Squares Discrimination Analysis (OPLS-DA) were used to identify the difference between pre- vs. post-operative sample set. T-test was used to confirm if the metabolites significantly different among groups at the univariate level (p < 0.05).

Results: Of the 70 patients, 31 (44.3%) were male and 39 (55.7%) were female. Median age was 63 years old (23 - 85). Majority of them were never-smokers (64.3%). Adenocarcinoma was the most common histology (91.4%). EGFR mutation was tested in 34 (48.6%) patients, of which, 22 (64.7%) of them were positive. OPLS-DA showed that pre- and post-operative metabolites distinguish into 2 different groups. Metabolomic analysis revealed tryptophan as the highest positive fold change comparing before and after surgery, together with other amino acids, carnitine, biogenic amines, and lipids (p<0.001). Glutamate was the only one metabolite that significant decreased after surgery. Kynurenine and tryptophan ratio were significant decrease in postoperative patients (p<0.001). The most significant fold change metabolites (tryptophan, lysophosphatidylcholine-acyl C16:0,carnitine,glutamate) were assembled for a predictive model which sum of total score more than 29 correspond to high probabilities prediction of the persistence of lung cancer in early stage lung cancer patients before and after surgery.

Conclusions: We identified a distinct cluster of significant metabolic biomarkers associated with early-stage NSCLC. These metabolites would be the potential important biomarker profile for early-stage NSCLC detection. A larger cohort is needed to be validated.