USING METABOLOMICS FOR H1N1 PNEUMONIA DIAGNOSIS AND PROGNOSIS

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Introduction: Non-targeted metabolomics is a technique based on analyzing as many endogenous metabolites as possible. It has shown great potential for finding biomarkers for disease diagnosis. Here, we applied nuclear magnetic resonance spectroscopy (NMR) and gas chromatography-mass spectrometry (GC-MS) to identify plasma metabolites that may facilitate early diagnosis of H1N pneumonia, and for prognostication of H1N1 outcome, particularly for those who are at highest risk of dying and providing a new approach to understanding the pathophysiology of the disease.

Objectives: We hypothesize that the plasma metabolomic profiles will be different in H1N1 pneumonia patients who die of H1N1 infection ≤ 90 days after hospital admission vs. age- and sex-matched patients with H1N1 who survived > 90 days. Our objective is to test this hypothesis using a retrospective-prospective nested cohort metabolomics comparison of H1N1 patients (survivors vs non-survivors).

Methods: Plasma samples (n=21) were obtained from two H1N1 pneumonia patient cohorts comprised of seven non-survivors vs. fourteen age- and sex-matched survivors. We conducted a non-target analysis and obtained 273 (GC-MS) and 54 (NMR) metabolite peaks, and from these, we identified 56 and 25 biomarker candidate metabolites showing significant differences between these two groups for GC-MS and NMR, respectively. We used unsupervised and supervised multivariate statistical analyses, including principal component analysis (PCA) and orthogonal partial least squares-discriminant analysis (OPLS-DA), to identify significant metabolic discriminations.

Results: By analyzing non-targeted NMR and GC-MS metabolomics datasets, we found that there were metabolomics footprints in plasma that discriminate the two H1N1 pneumonia cohorts. Preliminary results indicate that a statistically significant separation in metabolic profiles exists between H1N1 pneumonia survivors > 90 days vs. non-survivors ≤ 90 days. Our results indicated that NMR methodology was effective (p = 0.017) to quantitatively detect abundant plasma metabolites in both groups whereas the GC-MS methodology was even better (p= 0.0001) for selectively detecting more discriminating features compared to NMR. OPLS data from both NMR and GC-MS demonstrated a metabolic pattern that clearly separated dead patients from those that survived with a higher predictive power (Q2) for GC-MS (Q2=0.852) than NMR (Q2=0.597).
Figure 1. OPLS-DA plot of H1N1 plasma metabolomics profiles determined by NMR

Figure 2. OPLS-DA plot of H1N1 plasma metabolomics profiles determined by GC-MS