Development of Chemical Isotope Labeling LC-MS for Human Serum Metabolome Profiling from Dried Serum Spots

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Abstract

Dried serum spot (DSS) is a sampling method used to collect serum samples onto a special type of absorbent paper. After depositing serum to a spot, it is dried for storage and transport. The dried spot is then subject to analyte extraction and analysis. DSS has been used for a number of applications such as targeted drug analysis. DSS can potentially be a very useful sampling method for clinical metabolomics, considering that metabolomics studies often involve the use of many samples. DSS can be a more convenient and less expensive way of sample storage and transport. In this work, we report a workflow for performing serum metabolomics from DSS using a high-performance dansylation isotope labeling liquid chromatography mass spectrometry (LC-MS) platform [1,2].

In our work, three FTA DMPK cards, namely card A (red), card B (black) and card C (blue), were tested in order to select the optimal card suitable for performing serum metabolome profiling. The recoveries of dansylation labeling metabolites from three cards were compared. The recoveries of card A (87.5%) and card C (89.8%) were higher than card B (74.6%). More than 1000 peak pairs or putative metabolites were detected from serum deposited on card A and card C, while 880 peak pairs was detected from card B. From the combined results, 2036 unique peak pairs were detected. Among them, 1405 peak pairs were found from serum on card C and 1332 were observed from serum on card A. All of the above results suggested that card C was suitable for metabolome profiling because of high recovery and the optimal number of peak pairs detected.

We also compared the number of peak pairs detected in DSS stored at room temperature, -20℃ and -80℃. The results showed that the number of peak pairs detected from DSS over a period of storage were similar at three storage temperatures. The serum metabolites in DSS that were quantified by dansylation LC-MS were found to be stable for at least 7 days at room temperature and for 4 weeks when DSS was stored at a freezer (-20℃ and -80℃).

As an example of applications, the developed workflow was applied to metabolome profiling of DSS from healthy male (n = 10) and female (n = 10) subjects. PLS-DA score plots demonstrated the separation between the healthy male and female subjects. The important biomarkers distinguishing the male and female subjects were identified by matching the

significant metabolites with HMDB and a dansyl standard library. Other applications including the use of this method for disease biomarker discovery are currently underway.

In conclusion, we have developed a workflow of profiling the serum metabolomes from DSS. Our preliminary data suggest that dried serum spot may provide an alternative method to conventional sample collection for serum metabolomics.

References

(1) Guo, K.; Li, L. Anal. Chem. 2009, 81, 3919−3932.

(2) Wu, Y. M.; Li, L. Anal. Chem. 2012, 84, 10723−10731.