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Metabolic Profiling Associated with Autophagy of Human Placenta-Derived Mesenchymal Stem Cells by Chemical Isotope Labeling LC−MS

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Autophagy has been reported to have a pivotal role in maintaining stemness, regulating immune modulation and enhancing survival of mesenchymal stem cell (MSCs). However, the effect of autophagy on MSCs metabolism is largely unknown. Here, we report a workflow for examining the impact of autophagy on human placenta-derive MSC (hPMSC) metabolome profiling with chemical isotope labeling (CIL) LC−MS. Rapamycin or 3-MA was successfully induce or inhibit autophagy, respectively. Then ^{12}C- and ^{13}C-dansylation (Dns) labeling LC-MS was used to profile the amine/phenol submetabolome, 935 peak pairs and 52 metabolites were positively identified using Dns-metabolite standards library and 667 metabolites were putatively identified based on accurate mass match to metabolome databases. $^{12}C/^{13}C$-p-dimethylaminophenacyl (DmPA) bromide labeling LC-MS was applied to analyze carboxylic acid submetabolome, 4736 peak pairs were detected among which 33 metabolites were positively identified with DMPA metabolite standards library and 3007 metabolites were putatively identified. The analysis of PCA/OPLS-DA combined with volcano plots and Venn diagrams was used to determine the potential biomarkers among these metabolites. Pathway analysis results demonstrated that hPMSCs appeared to generate more ammonia, arginine, ornithine and 4-aminobutyraldehyd in arginine and proline metabolism pathway and utilized more pantothenic acid to synthesize acetyl-CoA to provide energy in beta-alanine metabolism pathway when autophagy was induced.In contrast, in inhibition of autophagy, the down-regulated biomarkers such as β-alanine, citrulline, L-proline, spermine, N-acetylputrescine and gamma-aminobutyric acid showed a reduced metabolic activity in both two metabolic pathways. Our research provides a more comprehensive and further understanding of hPMSC metabolism associated with autophagy.

Keywords: Mesenchymal stem cells, autophagy, metabolomics, chemical isotope labeling, LC-MS