Proteomic and redox-proteomic analysis of berberine-induced cytotoxicity in breast cancer cells

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Running Title: Proteomic analysis of berberine-induced breast cytotoxicity

Abbreviations:
1-DE, one-dimensional gel electrophoresis; 2-DE, two-dimensional gel electrophoresis; Ab, antibody; BBR, berberine; BSA, bovine serum albumin; CCB, colloidal coomassie blue; CHAPS, 3-[(3-cholamidopropyl)-dimethylammonio]-1-propanesulfonate; DCFH-DA, 2,7-dichlorofluorescin diacetate; ddH₂O, double deionized water; DIGE, differential gel electrophoresis; DTT, dithiothreitol; EDTA, ethylenediaminetetraacetic acid; FCS, fetal calf serum; MALDI-TOF MS, matrix assisted laser desorption ionization-time of flight mass spectrometry; NP-40, Nonidet P-40; SDS, sodium dodecyl sulfate; TFA, trifluoroacetic acid

Key words: berberine, proteomics, 2D-DIGE, MALDI-TOF, breast cancer, redox proteomics
Abstract

Berberine is a natural product isolated from herbal plants such as *Rhizoma coptidis* which has been shown to have anti-neoplastic properties. However, the effects of berberine on the behavior of breast cancers are largely unknown. To determine if berberine might be useful in the treatment of breast cancer and its cytotoxic mechanism, we analyzed the impact of berberine treatment on differential protein expression and redox regulation in human breast cancer cell line MCF-7 using lysine- and cysteine- labeling two-dimensional difference gel electrophoresis (2D-DIGE) combined with mass spectrometry (MS). This study demonstrated 96 and 22 protein features that were significantly changed in protein expression and thiol reactivity, respectively and revealed berberine-induced cytotoxicity in breast cancer cells involves dysregulation of protein folding, proteolysis, redox regulation, protein trafficking, cell signaling, electron transport, metabolism and centrosomal structure. Our work shows that this combined proteomic strategy provides a rapid method to study the molecular mechanisms of berberine-induced cytotoxicity in breast cancer cells. The identified targets may be useful for further evaluation as potential targets in breast cancer therapy.

Graphical abstract