The effects of cisplatin on the metabolome of ovarian cancer cells by using LC-MS

Sanad Alonezi

Prince Sultan Military Medical City, Saudi Arabia

Abstract

In this work, liquid chromatography-mass spectrometry (LC-MS) with zwitterionic HILIC material (ZIC-pHILIC) was used to analyze the intracellular metabolomic spectrum of the human ovarian cancer cell line A2780 and the cisplatin resistance cell line A2780CR, in which cisplatin was used to treat the cells at IC50 and IC20 concentrations. The cisplatin-sensitive cells were as expected more sensitive to cisplatin than the resistant cells with IC50 values of 4.9 and 10.8 µg/mL, respectively. Data extraction was carried out with MZmine 2.14 with metabolite searching against an in-house database. The data were analyzed using the univariate and multivariate principal component analysis (PCA) and Orthogonal projections to latent structures discriminant analysis (OPLS-DA) methods. There was clear discrimination between the controls and the cisplatin treated samples on the basis of PCA and OPLS-DA. The results demonstrated that the intracellular metabolomic changes induced by cisplatin in the cisplatin-sensitive cells led mostly to reduced levels of amino acids such as acetylcarnitine, phosphocreatine, L-Arginine, L-Ornithine, L-Proline and Glutathione disulfide as well as to increased levels of tryptophan and methionine. A number of biochemical metabolites were also significantly different between the cisplatin-sensitive and cisplatin-resistant cells based on the effect of cisplatin, with cisplatin-resistant cells presenting increased levels of L-Lysine, and decreased levels of N-Acetyl-L-glutamate, and 2-Oxobutanoate. Overall, this study proposes that mass spectrometry-based metabolomics can be a useful tool in pharmacological studies of the mechanism of action of drugs at a cellular level.

Biography

Sanad Alonezi received his Bachelor's Degree in Pharmaceutical Sciences from KSU in 2003 and MSc from KSU, Saudi Arabia. He holds PhD in Pharmaceutical analysis from university of Strathclyde in 2017 (UK). He is a consultant pharmacist at PSMMC. He has a strong interest in areas of research involve high resolution mass spectrometry and chromatography applied to metabolomics.

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