

Metabolomics in cancer research – investigation of the tricarboxylic acid cycle with mass spectrometry

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The tricarboxylic acid (TCA) cycle is one of the main energy production processes of the cells. During the cycle, the energy obtained from the decomposition of glucose is stored in the forms of GTP, NADH and FADH₂.

Tumour cells use up the glucose through the glycolysis pathway 10-50 times faster than normal cells [1]. According to the Warburg's theory the cancer cells take away glucose from normal cells, therefore inhibition of glucosetake-up results in cancer cell reproduction slow-down. One important marker of the cancer cells is the α -hydroxyglutarate [2] which is produced instead of α -ketoglutarate in the TCA cycle and this way the cycle is inhibited.

In order to model this process, normal and cancer cells were fed with isotope-marked carbohydrates, thus one can measure the ratio of glucose used up in the different metabolic cycles, respectively.

Undoubtedly, the various chemical properties of metabolites represent a great challenge in their

identification in cell cultures. Therefore, a high performance liquid chromatography (HPLC) tandem mass spectrometric (MS/MS) method has been developed for the simultaneous determination of nineteen glycolytic and tricarboxylic acid (TCA) cycle intermediate as well as amino acids.

These target compounds are highly polar, thus they were separated on a HILIC HPLC column and simultaneously determined by triple quadrupole MS/MS using multiple reaction monitoring. Calibration curves were made for the target compounds in standard stock solutions and the LOQ was calculated.

References:

1. O. Warburg, *Science*, 123, 1956, 309-314.
2. D. Ye, S. Ma, Y. Xiong, K.-L. Guan, *Cancer Cells*, 23, 2013, 274-276.