metabolic signatures of lung cancer unveiled by NMR-based metabonomics

cláudia rocha[1], antónio barros[2], brian goodfellow[1], ana gil[1], isabel carreira[3], j. bernardo[4], l. carvalho[3,4], iola duarte[1]

[1] department of chemistry & CICECO, university of aveiro
[2] department of chemistry & QOPNA, university of aveiro
[3] university of coimbra
[4] university hospitals of coimbra

By providing a non-selective survey of a wide range of endogenous metabolites and of their variations upon different pathological conditions, metabonomics is exquisitely valuable in disease diagnosis and follow up. We have applied this approach to investigate the metabolic signatures of primitive lung cancer, through the analysis of tissues and biofluids by ^{1}H Nuclear Magnetic Resonance (NMR) spectroscopy combined with multivariate statistics. Tumour and non-involved adjacent tissues, collected after surgical resection and directly analysed by High Resolution Magic Angle Spinning (HRMAS) NMR, could be clearly discriminated and putative biomarkers of malignancy were highlighted. Moreover, consistent metabolic differences were found between adenocarcinoma, carcinoid and epidermoid tumours, adding valuable knowledge on the biochemistry of different histological types of bronchial-pulmonary carcinomas, not available through conventional histopathology. We have also applied NMR-based metabonomics to blood plasma and urine from lung cancer patients and a control group of healthy individuals. Multivariate modelling of spectroscopic data produced very good discrimination between the two groups, with sensitivity and specificity levels above 90%. In spite of the high inter-individual variability, a number of metabolites were found to be consistently altered in the biofluids of patients relative to control subjects, therefore suggesting a systemic metabolic signature for lung cancer and showing the potential of NMR-based metabonomics for the minimally invasive detection and monitoring of the disease. It should also be noted that whereas some of the metabolites found to be altered in tissues and biofluids related to known cancer biochemical hallmarks, such as the Warburg effect, increased glutaminolysis, and deregulated lipid metabolism, others, like elevated short chain fatty acids and creatinine in urine, were unexpected, paving the way to formulate new pathophysiological hypotheses.

Multivariate modelling of the urinary profiles of lung cancer patients and healthy controls