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Blood molecular profile to predict genotoxicity from exposure to antineoplastic drugs – a comparison with cytokinesis-block micronucleus assay results

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Gentoxicity is an important information that should be included in human biomonitoring programmes design. Cytogenetic methods are usually laborious and time-consuming, therefore new molecular methods development is an added value. The aim of this study was to evaluate if the molecular profile of previously frozen whole blood as acquired by Fourier Transform Infrared (FTIR) spectroscopy, allow to assess genotoxicity in occupational exposure to antineoplastic drugs in hospital professionals, as obtained by the lymphocyte cytokinesis-block micronucleus (CBMN) assay. It was considered peripheral blood from hospital professionals occupationally exposed to antineoplastic drugs (n = 46) and from a non-exposed group (n = 46). It was first evaluated the metabolome from defrosted whole blood by methanol precipitation of macromolecules as haemoglobin followed by centrifugation. The metabolome molecular profile resulted in 3 ratios of spectral bands significantly different between the exposed and non-exposed group ($p<0.01$) and a spectral principal component-linear discriminant analysis (PCA-LDA) model enabling to predict exposure with 73% accuracy. After optimization of the dilution conditions of defrosted whole blood, it was also possible to obtain a higher number of significant ratios of spectral bands, i.e. 10 ratios significantly different at $p<0.001$, pointing the method high sensitivity and specificity. Indeed, the PCA-LDA model based on the molecular profile of whole blood enabled to predict the exposure at an accuracy, sensitivity and specificity of 92%, 93% and 91%, respectively.

All this was achieved based on 1mL of defrosted blood, in a high-throughput mode, i.e., based on the simultaneous analysis of 92 blood samples, in a simple and economic mode. The method presents therefore very promising potential for high-dimension screening of genotoxic effects from exposure to genotoxic substances.

Keywords:
Molecular profile, FTIR-spectroscopy, Genotoxicity, Cytokinesis-blocked micronucleus assay, blood.