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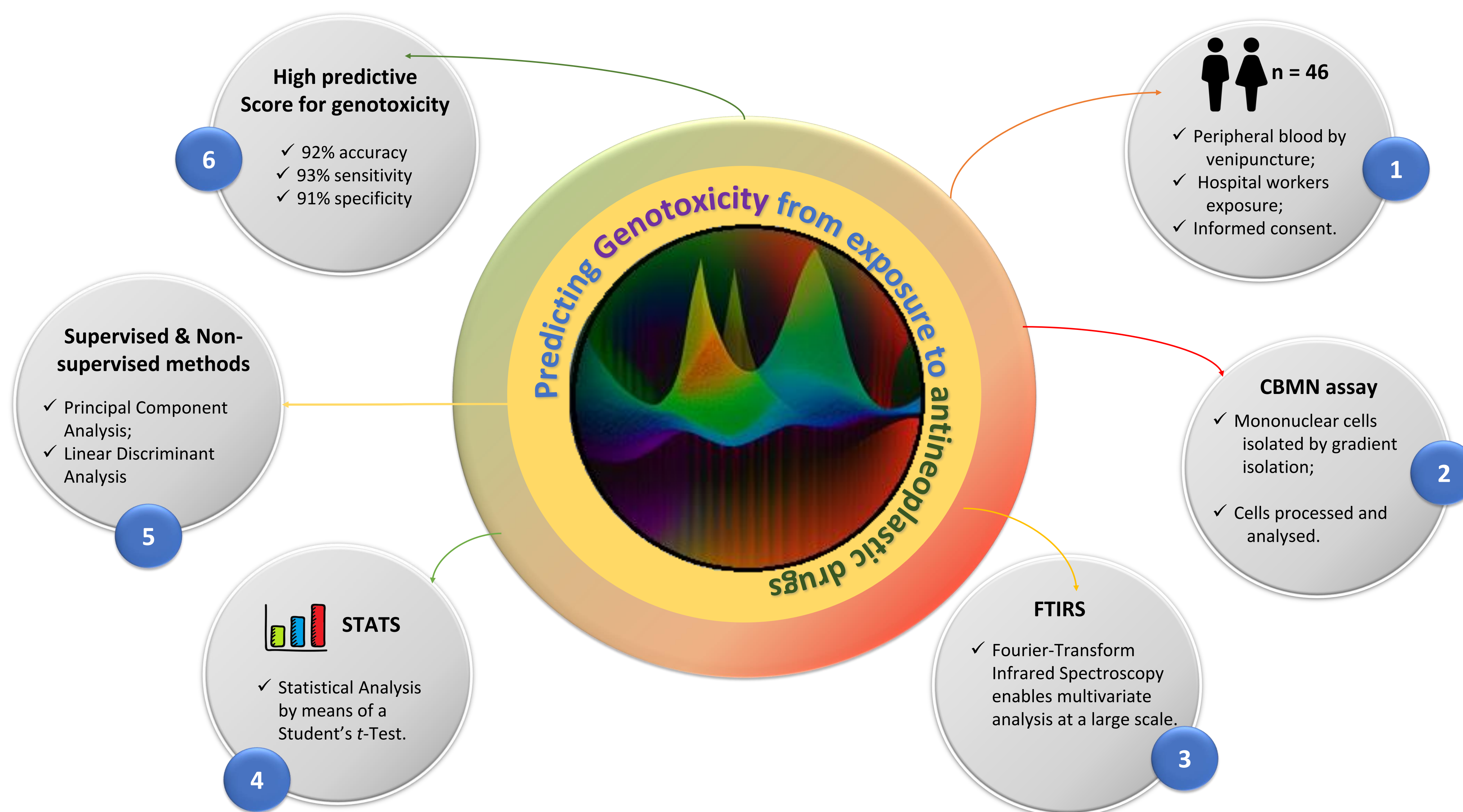
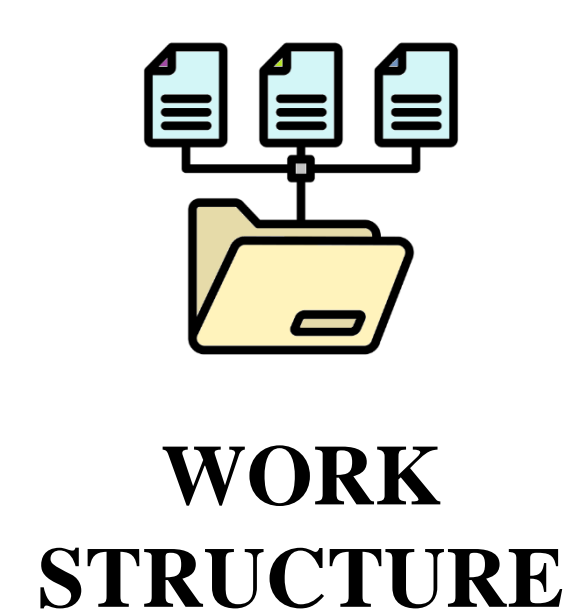
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## Genotoxicity

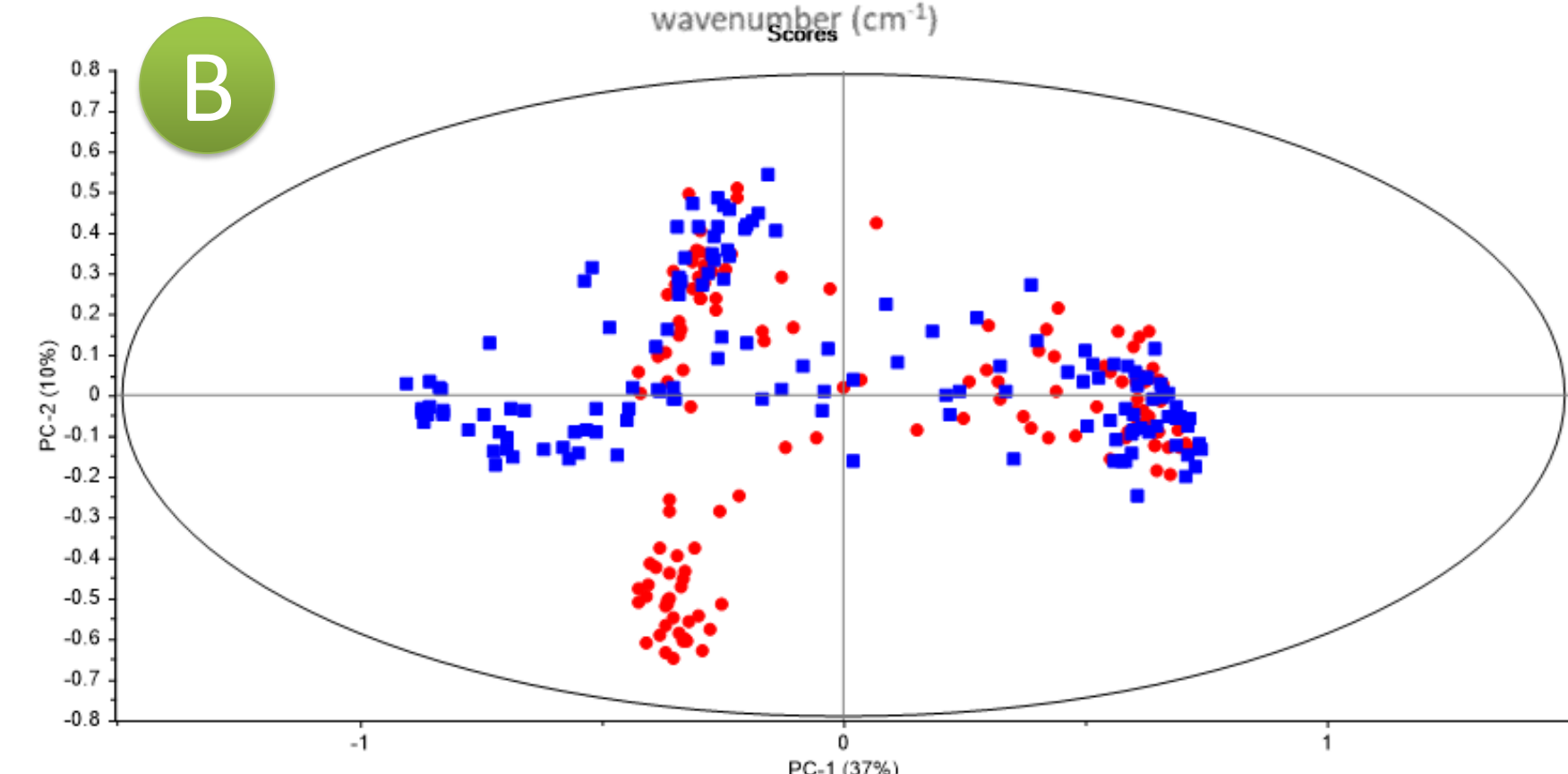
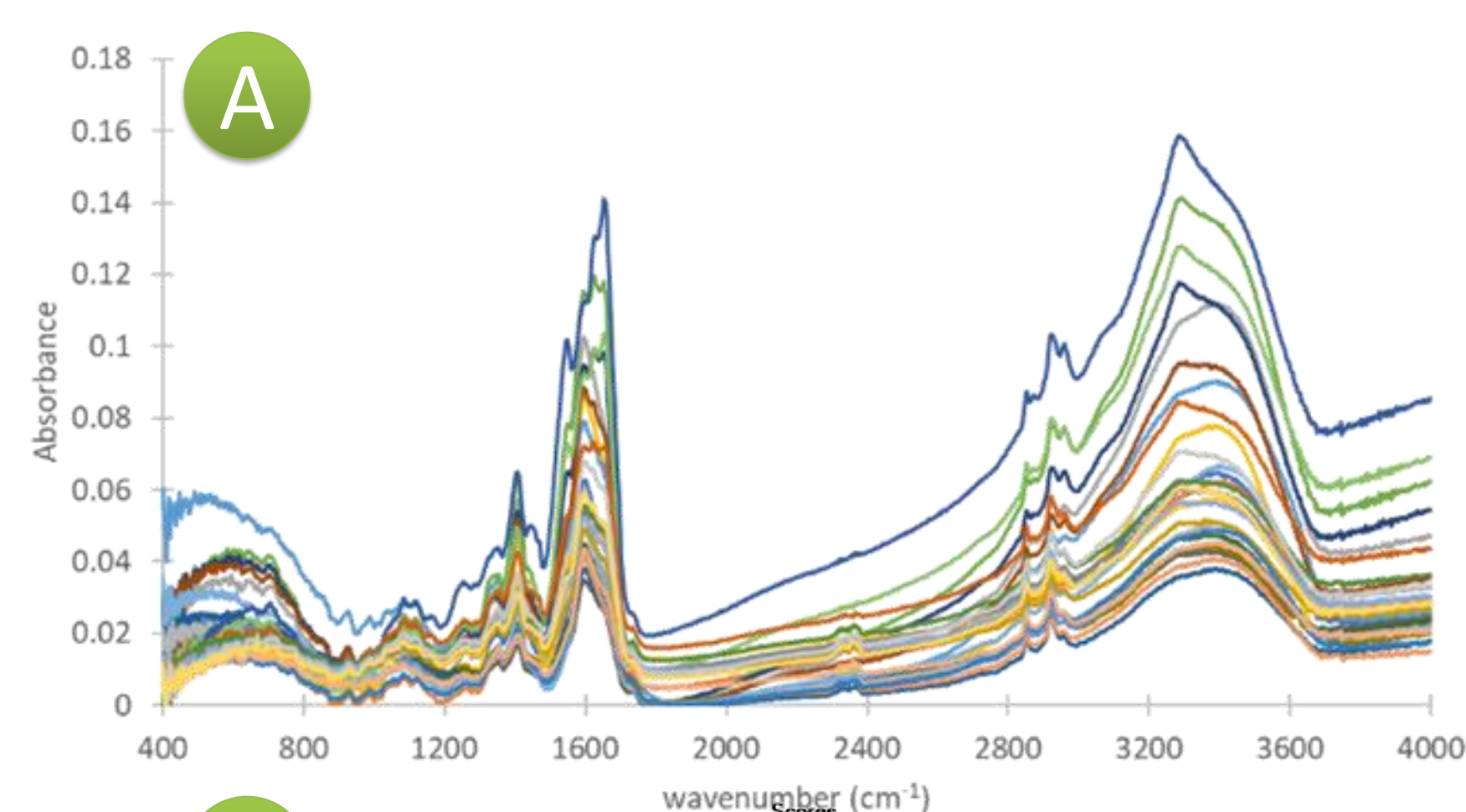
Genotoxicity [1] is an important information that should be included in human biomonitoring programs design [2]. Cytogenetic methods are usually laborious and time-consuming [3-5], therefore, development of new molecular methods is an added value.



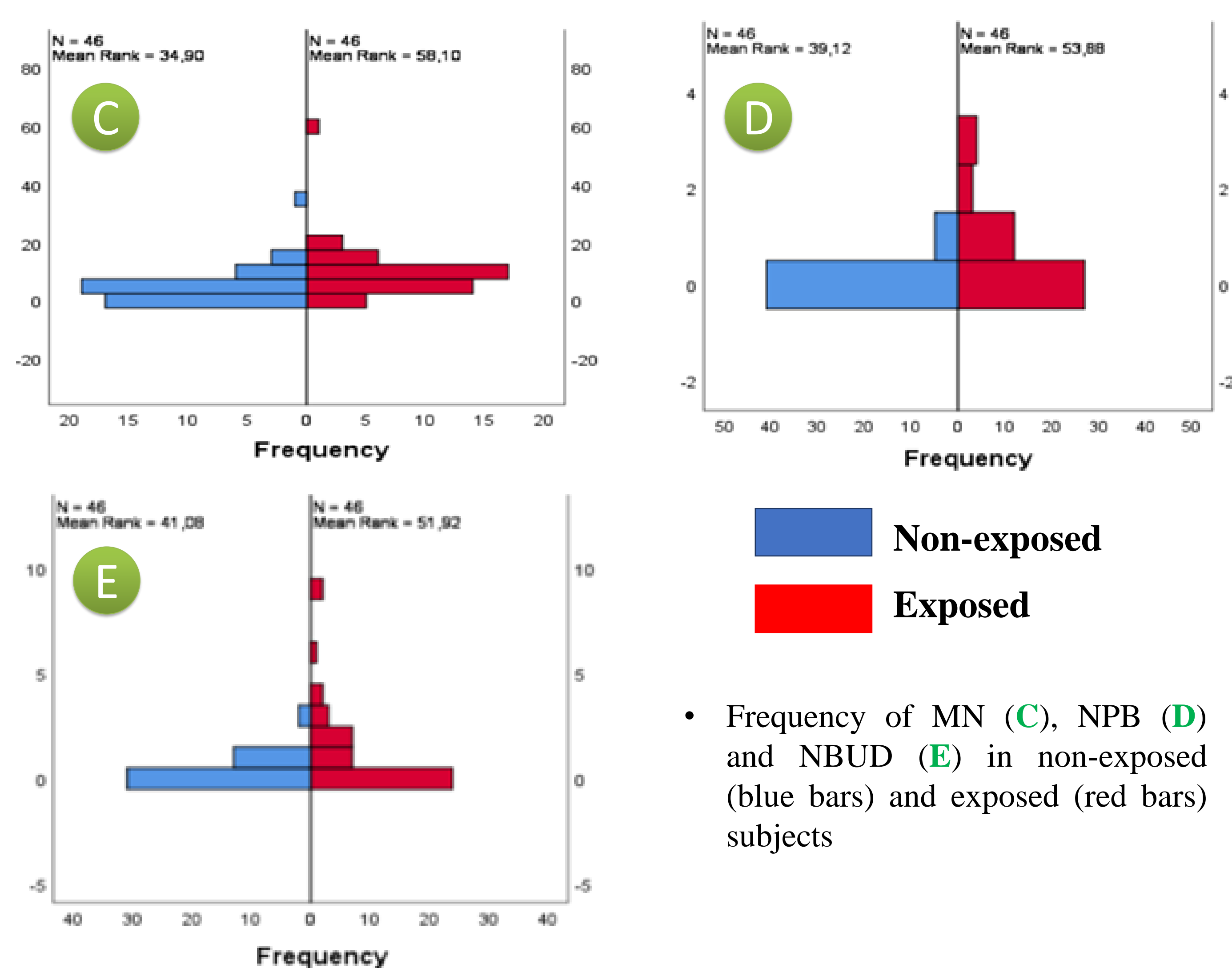
**The aim of this study** was to evaluate if the molecular profile of previously frozen whole blood acquired by Fourier Transform Infrared (FTIR) spectroscopy, allows to assess genotoxicity in occupational exposure to antineoplastic drugs in hospital professionals, as obtained by the lymphocyte cytokinesis-block micronucleus (CBMN) assay.



## RESULTS



- Example of spectra without pre-processing of methanol-based extracts from defrosted whole blood (A) and PCA based on normalised second derivative spectra of exposed (blue) in relation to non-exposed volunteers (red) (B).



- Frequency of MN (C), NPB (D) and NBUD (E) in non-exposed (blue bars) and exposed (red bars) subjects



## CONCLUSIONS

MIR spectroscopy enabled to capture the effect of individual exposure to genotoxic compounds on defrosted whole blood, non-centrifuged nor pre-processed with methanol, diluted only at 1/40 in NaCl solution, considering the normalized second derivative spectra between the region of 600 to 1300  $\text{cm}^{-1}$ . This resulted in encouraging predictive model results with an accuracy, sensitivity and specificity of 92%, 93% and 91%, respectively. As these resulted from analyses conducted with less than 1  $\mu\text{l}$  of whole blood, the study presents very promising outputs for a future and robust genotoxicity monitoring platform, being able to be applicable at a large scale.



## ACKNOWLEDGEMENTS

This work was supported by Instituto Politécnico de Lisboa under grant IDI&CA/IPL/2017/GenTox/ESTeSL, and by Fundação para a Ciência e a Tecnologia, Portugal, under grant DSAIPA/DS/0117/2020. The human biomonitoring had financial support given by Portuguese Authority of Working Conditions (Project reference: 036APJ/09).

## BIBLIOGRAPHY

- [1] N. Ren, M. Atyah, W.-Y. Chen, C.-H. Zhou, The various aspects of genetic and epigenetic toxicology: testing methods and clinical applications, *J. Transl. Med.* 15 (2017) 110. <https://doi.org/10.1186/s12967-017-1218-4>.
- [2] M. Hayashi, Opinion: regulatory genotoxicity: past, present and future, *Genes Environ.* 44 (2022) 13. <https://doi.org/10.1186/s41021-022-00242-5>.
- [3] J.C. Barrett, H. Vainio, D. Peakall, B.D. Goldstein, 12th meeting of the Scientific Group on Methodologies for the Safety Evaluation of Chemicals: susceptibility to environmental hazards., *Environ. Health Perspect.* 105 (1997) 699–737. <https://doi.org/10.1289/ehp.97105s4699>.
- [4] J.M. Battershill, K. Burnett, S. Bull, Factors affecting the incidence of genotoxicity biomarkers in peripheral blood lymphocytes: impact on design of biomonitoring studies, *Mutagenesis.* 23 (2008) 423–437. <https://doi.org/10.1093/mutage/gen040>.
- [5] C. Ladeira, S. Viegas, Human Biomonitoring – An overview on biomarkers and their application in Occupational and Environmental Health, *Biomonitoring.* 3 (2016). <https://doi.org/10.1515/bimo-2016-0003>.