The Action of Two Different Chemotherapeutic Drugs on a Highly Resistant Cell Line Analysed as a Function of the Cell Cycle by Means of FTIR MS.

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The FTIR spectral profiles of Caki-2 cells, a highly chemo-resistant renal cell carcinoma cell line exposed to either Paclitaxel or 5-FU, were analysed as a function of the cell cycle in order to determine whether the differential response triggered by these two drugs, known to act via distinct modes of action, could be revealed by means of FTIR spectroscopy. Although Derenne *et al.*(*1*) have recently shown that the influence of the cell cycle is considerably small compared with the overall effect of the drug on PC-3 cells cultured *in-vitro*, our study aimed to a) demonstrate the capability of FTIR spectroscopy for retrieving the cell cycle phase of untreated and drug-treated cells via the construction of a robust SVM(*2*) b) highlight the metabolic modifications induced by the drugs also in the S-phase of development and c) determine whether there could be a marker of preferential sensitivity to any of the drugs in order to pave the path to a personalised treatment that could minimize the side effects faced by a cancer patient under treatment. The spectroscopic profiles of drug-treated Caki-2 cells showed that there is a consistent biochemical response among all the cell cycle phases and irrespective of the chemotherapeutic compound used to treat the cells. Interestingly, these biochemical features are related to the accumulation of lipids in cells undergoing apoptosis(*3-5*). The construction of a linear SVM involving a pool of data of control and drug-treated cells revealed that, even though the cell cycle itself is not the clustering trend of the asynchronous culture of Caki-2 cells exposed to either Paclitaxel or 5-FU, it is in fact possible to classify these cell cycle phases with an average accuracy of 77.98%; thus, we believe that it is still too early to completely rule out the influence of the cell cycle while analysing chemotherapy drugs on a single cell level.

References

1. Derenne, A., Mignolet, A., and Goormaghtigh, E., FTIR spectral signature of anticancer drug effects on PC-3 cancer cells: is there any influence of the cell cycle?, *Analyst* 138, 3998-4005(2013).
2. Jimenez-Hernandez, M., Hughes, C., Bassan, P., Ball, F., Brown, M. D., Clarke, N. W., and Gardner, P., Exploring the spectroscopic differences of Caki-2 cells progressing through the cell cycle while proliferating in vitro, *Analyst* 138, 3957-3966 (2013).
3. Liu, K. Z., Jia, L., Kelsey, S. M., Newland, A. C., and Mantsch, H. H., Quantitative determination of apoptosis on leukemia cells by infrared spectroscopy, *Apoptosis* 6, 269-278 (2001).
4. Gasparri, F., and Muzio, M., Monitoring of apoptosis of HL60 cells by Fourier-transform infrared spectroscopy, *Biochem J* 369, 239-248 (2003).
5. Blankenberg, F. G., Katsikis, P. D., Storrs, R. W., Beaulieu, C., Spielman, D., Chen, J. Y., Naumovski, L., and Tait, J. F., Quantitative analysis of apoptotic cell death using proton nuclear magnetic resonance spectroscopy, *Blood* 89, 3778-3786 (1997).