A Raman-based approach for detecting circulating tumor cells.

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KEY WORDS: Raman spectroscopy, CTCs, deuterium, vibrational tag

Circulating tumor cells (CTCs) are a rare subgroup of cells that detach from the primary solid tumor and circulate in the bloodstream of cancer patients. These cells act as a seed for metastases; moreover, they maintain the primary tumor heterogeneity and mimic tumor properties. All these features make CTCs good candidates to be used as clinical biomarker for patient diagnosis, prognosis and treatment. Nevertheless, the available methods of CTC isolation are far from ideal. They do not work with all tumor types, and the isolated cells are not always viable thus preventing their analysis and development of personalized treatment regimen. Thus, efficient method to isolate viable CTCs that work for all tumor types is an urgent medical need. Here, we used deuterium as vibrational tag to develop a new CTCs detection method based on Raman microspectroscopy potentially able to detect any type of CTCs. In particular, we exploited the capacity of cancer cell to internalize and metabolize glucose 5-10 faster than normal cell, the so-called Warburg effect. Normal prostatic cells (PNT2), cancer prostatic (PC3) and hepatic (HepG2) cells were used as in vitro model. Cells were cultured in presence of 25mM deuterated glucose for 48h and then analyzed by Raman microspectroscopy [1]. The typical deuterium Raman band at 2100 cm-1 was present in the spectra of PC3 and HepG2 cells, but not in PNT2 spectra. These results indicate the presence of Warburg effect in our cellular model and that cancer cells can be differentiated from normal cells following glucose metabolism. To simulate the presence of CTCs in blood, PC3 and HepG2 cells were co-cultured with white blood cells isolated from healthy donor blood in presence of deuterated glucose. The deuterium Raman signal was observable only in the spectra of PC3 and HepG2 cells. Our data demonstrate that cancer cells can be distinguished from healthy cells independently from EpCAM expression just exploiting the glycolytic metabolism also when they are in the same media. These results shed a light on the possibility to develop new CTCs detecting methods using label-free approach based on Raman spectroscopy.

1. Managò S., Valente C., Mirabelli P., Circolo D., Basile F., Corda D. and De Luca A.C, 2016. A reliable Raman-spectroscopy-based approach for diagnosis, classification and follow-up of B-cell acute lymphoblastic leukemia. *Sci Rep*. 19, 6:24821.