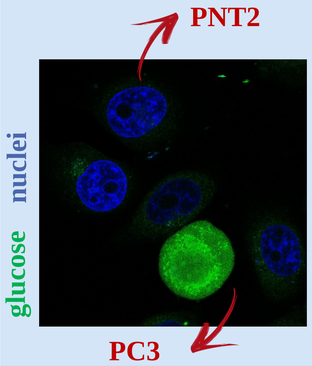
A new combined Raman and polarization holographic approach for sensing circulating tumor cells

Maria Mangini[1], Maria Antonietta Ferrara[2], Gianluigi Zito[2], Stefano Managò[1], Alberto Luini[1], Giuseppe Coppola[1] and Anna Chiara De Luca[1]

[1]Institute of Biochemistry and Cellular Biology, National Research Council, Naples, Italy. [2] Institute of Applied Sciences and Intelligent Systems, National Research Council, Naples, Italy.

Contact: annachiara.deluca@ibbc.cnr.it

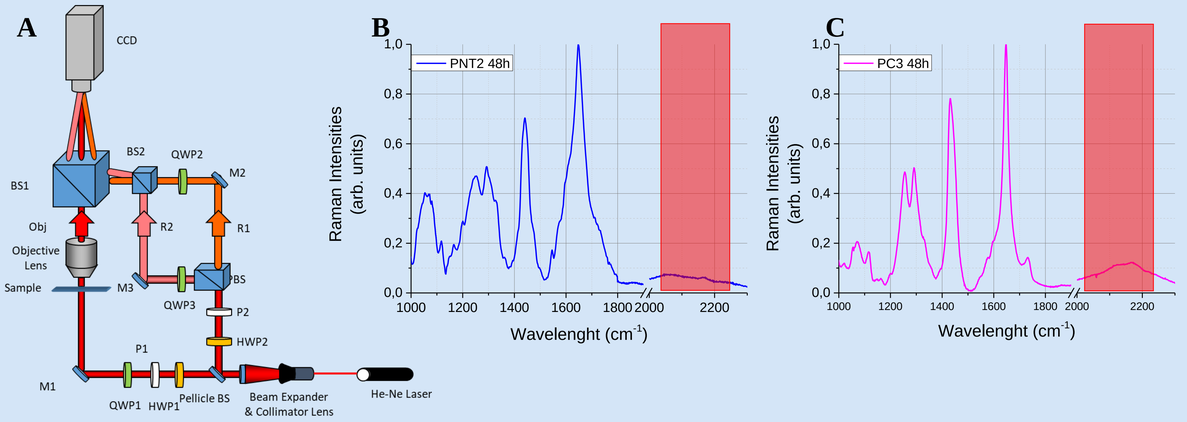
Abstract



The Warburg effect describes the ability of cancer cells to internalize and metabolize glucose 5-10 faster than healthy cells. Here in, we aim to exploit this cancer cell feature to develop a new method to detect circulating tumor cells (CTCs) based on Raman spectroscopy and cell birefringence analysis.

Confocal images of a co-culture of healthy (PNT2) and cancer (PC3) prostatic cells treated with fluorescent glucose (green). The figure shows the Warburg effect present in PC3 as these cells internalize more fluorescent glucose than PNT2.

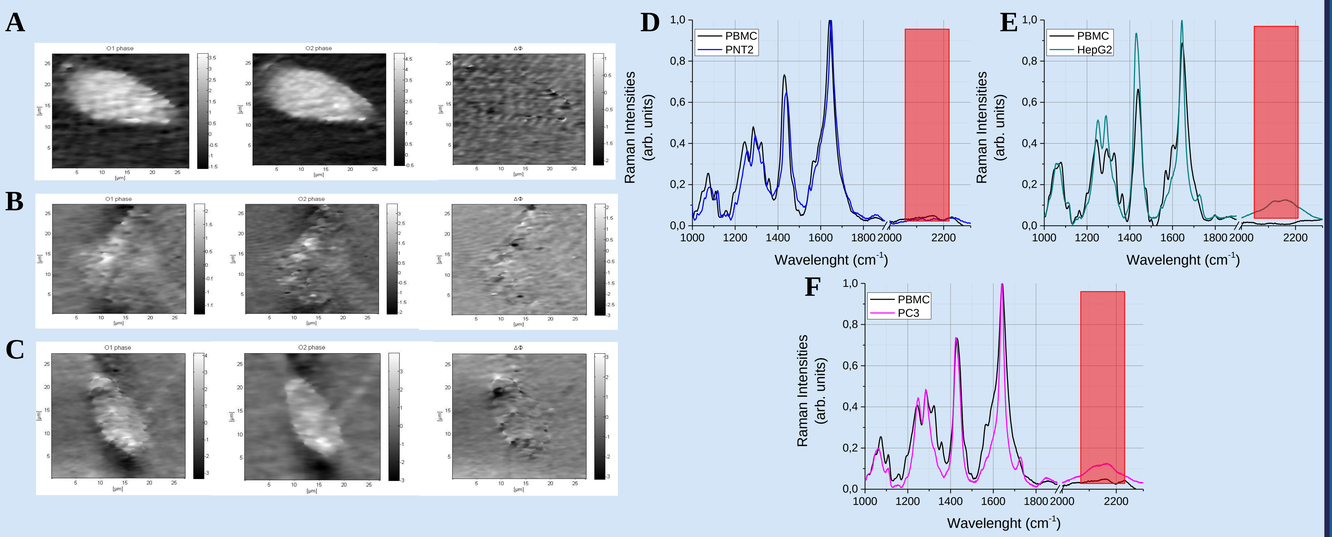
Methods



PNT2 and PC3 cells were cultured for 48 h in medium containing 25mM deuterated glucose (for Raman microscopy) or standard glucose (for birefringence analysis). In (**A**) the set-up of the instrument used for the cell biriefringence analysis is shown. It is based on two Mach-Zender interferometers obtained by splitting the reference beam in two orthogonal beams. These two reference beams interfere with the object beam polarized at 45°.

PNT2 (**B**) and PC3 (**C**) Raman spectra are shown. The deuterium signal appears in the silent zone of the cell spectra at 2100 cm^{-1} and is highlighted in red windows. The band of deuterated glucose was observable only in cancer cell (**C**) spectra.

Results



PNT2 cells (**A**) have an homogeneous cell birefringence, instead in PC3 (**B**) and HepG2 (**C**) cells there area with a different degree of birefringence due to the presence of granules wiht a high content of glucose.

In order to mimic the presence of CTCs in blood, PNT2 (**D**), PC3 (**E**) and HepG2 (**F**) cells were mixed with white blood cells (PBMC) extracted from healthy donor blood. The co-cultures were maintened for 48 h in medium containg deuterated glucose and analyzed by Raman microscopy. The deuterium signal was present only in the spectra of tumoral cells (**E**,**F**).

Conclusions and future perspectives

- Raman spectroscopy and the analysis of cell birefringence allow to follow glucose metabolism and to distinguish cancer from healthy cells. This tools are useful to set up new methods for CTCs detection.
- In future the analysis will be extented to other cancer cell lines and the birefringence analysis will be carried out also on PBMC-cancer cell co-culture.

References and acknowledgement

(1) Managò S., et al. 2016. A reliable Raman-spectroscopy-based approach for diagnosis, classification and follow-up of B-cell acute lymphoblastic leukemia. *Sci Rep*. 19, 6:24821

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