Squeezing Prostate Cancer

Abstract

Currently, the diagnosis of prostate cancer is achieved by annual PSA screening and digital rectal examination (DRE). However, the lack of sensitivity and specificity of PSA as a tool to diagnose prostate cancer, as well as its inability to predict the clinical aggressiveness of a tumour have limited its utility. In our work we search for diagnostic signatures for prostate cancer which might also provide information on the aggressiveness of the cancer. To this end we have used reflection mode Fourier transform infrared photoacoustic spectroscopy (FTIR-PAS), Raman Laser Tweezers and atomic force microscopy (AFM) to study the applicability of these techniques to discriminate between prostate cancer cells of differing invasiveness and non-cancer prostate cells. Results of our work have shown that the cells can be discriminated spectroscopically using FTIR-PAS2 and Raman Laser Tweezers.3 Sensitivities and specificities of >90% and 98% were achieved using Raman Laser Tweezers and Principal component-linear discriminate analysis (PCLDA).

In addition, we have investigated the hypothesis that the mechanical properties of cells might be a useful marker for cancer progression. It has been suggested that cancer cells are less stiff than non-cancer cells and that invasive cancer cells are less stiff than non-invasive cancer cells. We have determined the stiffness of non-cancerous prostate cells (BPH), non-invasive prostate cancer cells (LNCaP) and highly invasive prostate cancer cells (PC-3) using an atomic force microscope (AFM).5 We have shown that prostate cancer cells were more easily deformed than non-cancer cells. However, the highly invasive PC-3 cells were stiffer than the non-invasive LNCaP.

The results revealed that the Young’s moduli decrease with indentation depth, but for each indentation range the trend is maintained and BPH, PC-3 and LNCaP can be discriminated based on their apparent Young’s moduli (Fig. 3). As hypothesised, the BPH cells are less easily indented and therefore exhibit a higher Young’s modulus than the tumorigenic LNCaP and PC-3 cells.

Importantly, the LNCaP and the PC-3 cell lines have been cultured in identical culture media but show significant separation, indicating that the separation is not due to the culture media but is related to the cells.

The underlying reasons for this differentiation is as yet unclear, but may be due to differences in cell morphology or biochemistry or a combination of both.

Squeezing, Hearing and Illuminating Prostate Cancer

Several studies have shown that cancer cells are more easily deformed than healthy cells and that highly aggressive cancer cells are more easily deformed than less aggressive cancer cells. It has also been suggested that the elastic properties of cancer cells play a major role in the metastatic process. Consequently, it has been hypothesised that elastic properties such a deformability of the cells could be used as a marker for metastatic potential.

Hearing Prostate Cancer

FTIR – Photoacoustic Spectroscopy

Photoacoustic spectroscopy (PAS) is an alternative to conventional IR spectroscopy and relies on the detection of acoustic waves generated as a result of the absorption of modulated light. (See schematic in Fig. 4) The amplitude of the PAS signal depends on the amount of absorbed energy that is converted to heat through non-radiative decay routes.

Principle component analysis separated the data into four distinct clusters representing the four different cell lines (Fig. 6). PC1 separates only BPH and PNT2-C2 whereas PC2 separates LNCaP, PC-3, and BPH/PNT2-C2. LNCaP appears to be the most distinct group.

Illuminating Prostate Cancer

Raman Laser Tweezers

Laser Tweezers enable the trapping of micron-sized particles, such as cells by virtue of radiant forces (see Fig. 7). We have combined Laser Tweezers with Raman spectroscopy to analyse single urological cells with reduced interference from the substrate and other cells.

Principal Component Analysis (PCA) and Linear Discriminant Analysis (LDA) were then used to classify spectra obtained for the different cell types. The results shown here were obtained for formalin fixed cells.

References

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Fig. 3: Apparent Young’s modulus for LNCaP (E = 287 ± 12 N m⁻², n = 52), PC-3 (E = 1451 ± 162 N m⁻², n = 53) and BPH (E = 2757 ± 1491 N m⁻², n = 51). Error bars represent the 95% confidence interval.

Fig. 9: PC-LDA plots obtained from formalin fixed cells (LNCaP, PC-3, BPH/PNT2-C2, MGH-U1/urethral (U) and BPH/LNCaP/PCT2/C8/MGH-U1/urethral (C)).