Identification of miRNAs associated with radioresistance in a prostate cancer model

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Purpose/Objective: High risk of tumour regrowth following treatment with radiation therapy for a subset of prostate cancer patients highlights the need for prognostic biomarkers. miRNAs are key regulators of cancer cell behavior that could control their response to ionizing radiation. Owing to their availability in tissues, serum and urine, miRNAs are ideal candidates for the development of novel biological tests. This study aimed to identify key miRNAs associated with a radioresistant phenotype in cancer cells, as a prerequisite for the future development of a novel pre-treatment assay for the identification of radiotherapy prostate cancer patients at risk of biochemical failure.

Materials and Methods: A dual approach was used for the identification of candidate miRNAs associated with radioresistance: (1) an isogenic radiation resistant model was generated using the 22Rv1 (primary) prostate cancer (CaP) cell line through weekly exposure to 2-Gy fractionated ionising radiation. (2) chronically hypoxic 22Rv1 cells (48hrs) were used as an additional model for radioresistance. miRNA profiling of radioresistant and wild type cells was performed using the Exiqon miRCURY array and overlapping profiles identified 105 significantly differentially expressed miRNAs in RR22Rv1, when compared to both parent and age-matched controls. A total of 12 miRNA were differentially expressed in chronically hypoxic compared to normoxic 22Rv1 cells. Three candidate miRNAs were associated with a radioresistant phenotype across the models: miR200a, miR210 and miR4284. Functional validation of these candidates is currently under way.

Conclusions: This study demonstrates a role for miRNAs in the radioresponse of prostate cancer cells and highlights their potential for the development of novel prognostic biomarkers for radiotherapy prostate cancer patients.

Image analysis for enhancing the bladder-prostate junction on radiotherapy planning CT images

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Purpose/Objective: Organ preservation of muscle invasive bladder cancer after external radiotherapy is an important outcome for those patients who are unresectable or chose not to have cystectomy. Geometric uncertainties due to pelvic organ movement and internal bladder motion present a major challenge in defining the true extent of the bladder on computerised tomography (CT) images. This is complicated further by a lack of soft tissue contrast on CT images at the bladder prostate junction (BPJ) where significant clinical experience is required to interpret and ensure that the dose to the prostate remains within acceptable limits. The aim of this study was to investigate the use of image analysis for enhancing the BPJ on CT images used for RT planning and thereby allow simple image thresholding to produce reliable estimates of the clinical target volume (CTV). This has application in adaptive radiotherapy for automatically defining the bladder volume on cone-beam CT (CBCT).

Materials and Methods: Image data was acquired on a single slice General Electric (GE) HiSpeed Fx/i CT scanner (GE Medical Systems, Milwaukee, WI, USA) with 0.977 mm pixel resolution in the transaxial plane and a 2048 grey-level range. Five bladder cancer patients treated with a radiation dose of 52.5 Gy (20 fractions/4 weeks) at the Edinburgh Cancer Centre (ECC), were included in this study. Each patient received a 3 mm thick CT scan, with a presumed empty bladder, which was used to: define the target volume; define critical anatomical structures; determine the optimum radiation beam arrangement; and estimate the dose. Where possible CT scanning was performed twice weekly and repeat CT scans registered against bone on the corresponding planning scan using the GE Advantage fusion software. This resulted in 36 data sets, which were contoured by an experienced radiation oncologist and image analysis methods used to produce a new image set containing the enhanced BPJ.

Results:

On the 36 new data sets a threshold was set to extract the CTV, which included the bladder and BPJ. The variability