

21st World Congress on

RADIOLOGY & CANCER RESEARCH

August 27-28, 2018 | Toronto, Canada

Developing novel models to study radiobiological response in prostate cancer

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In the United Kingdom, prostate cancer is the most commonly diagnosed cancer in males. Recent sequencing studies have shown considerable intra-tumoral heterogeneity in the spectrum of somatic mutations associated with prostate cancer. Current pre-clinical models inadequately reflect these changes and there is an urgent need for tissue-derived models to support drug development/optimisation of therapies. Furthermore recent evidence indicates that treatment itself can alter the phenotypes of cancer cells and their expression of lineage-associated markers. To try to address some of these challenges we have set out to derive new pre-clinical models from mouse transgenic tumours and human tumour samples. Biopsies are obtained from pre and post brachytherapy treated prostate cancer patients as well as PTEN/p53 knock out mice. Prostate cells are then dissociated and co-cultured on a fibroblast feeder layer which has been pre-treated with Mitomycin C, with subsequent enrichment of luminal, basal and progenitor/stem-like cell using tailored media conditions. The efficacy of the approach is assessed by flow cytometry and imaging using a panel of cellular markers. Our methods for deriving and propagating primary cells from tissue samples have generated novel prostate cancer models which will now be subjected to further characterisation including genomic profiling and assessments of their responses to radiotherapy, anti-androgens. Ultimately it will be important to assess this in an *in vivo* setting to account for the impact of the tumour microenvironment.

Biography

Charles is a final year PhD student in Prof Ian Mills and Dr Suneil Jain Lab at Queens University Belfast. His PhD is developing novel models of prostate cancer from transgenic mice and human biopsies taken pre and post brachytherapy.

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