UCL / UCLH Biobank for Studying Health and Disease for the combination of markers with imaging for improved diagnosis of aggressive prostate cancer

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INTRODUCTION

UCL/UCLH Biobank for Studying Health and Disease

The UCL/UCLH Biobank for Studying Health and Disease supports research and promotes collaboration with internal and external researchers through the use of human biosamples and clinical data. Approximately 30,000 samples/year are collected from patients attending University College London Hospital (UCLH) NHS Foundation Trust, UCL Partner (UCLP) NHS Trusts and the Royal National Orthopaedic Hospital (RNOH) NHS Trust. Samples are collected from donors with a wide variety of different cancer types following an informed consent process. All donations to the Biobank are considered a gift for the benefit of other patients and future research. The Biobank is publicised to all new members of staff and students as part of their induction. Information are also available on the UCL website (http://www.ucl.ac.uk/biobank).

Project: combining markers with imaging for improved diagnosis of aggressive prostate cancer

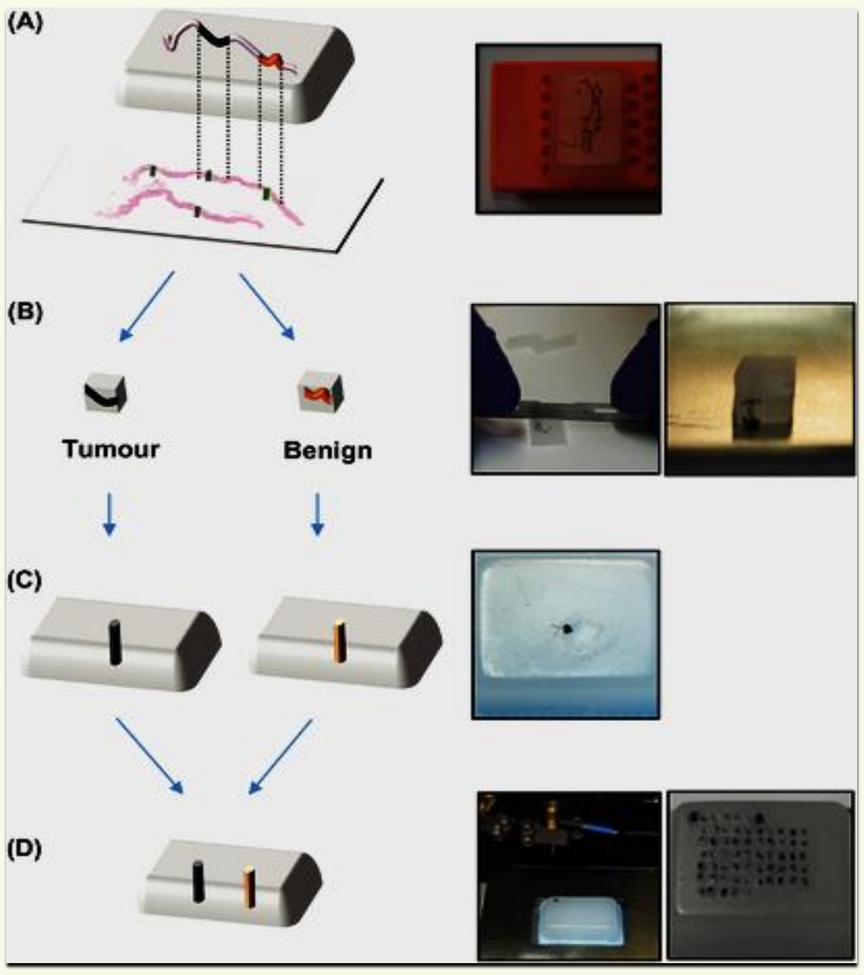
Prostate cancer is the most common cancer among men in the UK. Every year hundreds of thousands of men have a transrectal-ultrasound (TRUS) biopsy to see if they have the disease, but there are problems with this approach. TRUS biopsies miss around half of clinically important cancers, and they are uncomfortable for patients. In the last decade, different clinical trials have tested whether a MP-MRI (multi-parametric magnetic resonance imaging) scan before biopsy could identify men who might safely avoid a biopsy. The results showed that MP-MRI is an important technique for characterising and targeting the biopsy of suspected prostate cancer, as it reduces the number of unnecessary biopsies and efficiently detects clinically significant targets without over-diagnosing insignificant disease. Incorporating tissue biomarkers in the patient stratification process could further refine the emerging imaging-based patient pathways, but selecting molecules for such purposes requires their parallel testing in very small amounts of diagnostic tissue. Tissue microarrays (TMAs) constructed from prostate needle biopsies are a promising tool for high-throughput biomarker development and validation.
The main objective of this study lead by Dr Hayley Whitaker and her team was to prepare a TMA containing multiple non tumoural and tumoural areas from each patient and use it to find prognostic markers that could complement the data from the imaging analysis.

METHOD

To gain access to the human tissues stored in the Biobank, the group submitted the documentation required to the Biobank Ethical Review Committee (B-ERC), including:

- Biobank application form with a brief overview of the proposal.
- Evidence of HTA training, GCP training and Information Governance training
- Organogram of the group
- Standard Operating Procedures to demonstrate compliance with the policies on confidentiality, disposal, security, quality management, data protection, access, training, consent and audit of compliance set out by the Human Tissue Authority.

Once received ethical approval from the B-ERC, all the blocks and slides for each prostate cancer patient have been collected from the UCL Biobank. For the TMA preparation, the close partnership between UCL Biobank and the Pathology Core Facility at the UCL Cancer Institute has been fundamental. All the H&E slides for each patient have been scanned in the facility and expert uropathologists have identified the tumour and benign regions on the digital images. Then the corresponding areas were excised and embedded vertically into a new TMA block. TMA sections were then IHC-stained for the routinely used prostate cancer biomarkers and the results correlated with the Gleason grade of the original core and the MRI score.



TMA construction: Benign and malignant areas of 2 mm were identified within a biopsy core on H&E and selected for inclusion in the TMA (A). Each selected area was excised from the original block (B). The wax chips were re-positioned vertically, and then embedded in a new paraffin donor block (C). All the core segments were introduced into the final TMA block (D).

RESULTS

A total of 448 tissue blocks have been retrieved from UCL Biobank and 2240 cores were inserted in 7 different TMA blocks and analysed for routinely used prostate cancer biomarkers. There was a statistically significant difference in the staining intensity and number of positive cells between patient matched malignant and adjacent benign tissue. Moreover, some of the markers correlates with the likelihood of presence of cancer according to the MRI.

CONCLUSIONS

Tissue microarray technology allows rapid visualization of molecular targets in thousands of tissue specimens at a time. The speed of analyses is increased by more than 100-fold, and it is possible to study archival tissue specimens, usually not appropriate for other high-throughput genomic and proteomic tests. As all high-throughput analysis, the construction of TMA rely on the availability of a large and well characterized cohort of archival blocks. Using archival biopsy tissue stored in UCL Biobank, this team was able to construct tissue-selective microarrays from prostate biopsy samples for the purposes of parallel IHC and radiological biomarker validation. The IHC results obtained through this method were found to be highly reliable and significantly correlated with imaging data. These data have been published in The Prostate journal (Olivier et al., Immunohistochemical biomarker validation in highly selective needle biopsy microarrays derived from MP-MRI-characterized prostates, The Prostate, Aug 2018) where the Biobank has been acknowledged for its contribution. Moreover, this team has been involved in many donor engagement and publicity activities, such as:

- The London March for Men, Prostate Cancer UK
- CRUK Science Museum Lates
- UCL's Development and Alumni Relations Office (DARO) events

In the last decade MP-MRI has emerged as an important technique for characterizing and targeting the biopsy of suspected prostate cancer. If this approach is taken up across the UK, around 40,000 men each year could avoid having biopsies and their associated side-effects. Internationally, the impact of this innovation could be huge, as there are around 1 million TRUS biopsies carried out in Europe, and another 1 million in the USA, each year. Combining clinical results with molecular analysis could bring new insight in cancer mechanisms and biobanks and their archival tissues have a fundamental role in this process.

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