Early detection of prostate cancer by investigating the host peripheral immune response

Junjie Chai[1]
Xueying Mao[1], Ai Nagano[1], Claude Chelala[1], Edwina Burke[1], Daniel Berney[1], Jun Wang[1] and Yong-jie Lu[1]
[1] Barts Cancer Institute, Queen Mary University of London

Background & objectives

Prostate cancer (PCa) is the second most prevalent cancer globally, with the prostatic specific antigen (PSA) being the most popular tool for its diagnosis followed by painful tissue biopsies. However, PSA has a low specificity leading to unnecessary biopsies and over-diagnosis of latent PCa. Developing more accurate non-invasive biomarkers for early diagnosis of aggressive PCa is required. The peripheral immune system can potentially act as a signal amplifier for tumour cells at early tumour development, especially when being exposed to the circulating tumour cells (CTCs) and other tumour products entering the circulation. Yet, the peripheral immune response to PCa has not been completely explored. The objectives of this study are to characterize the host peripheral immune response to PCa and evaluate its potential diagnostic value as a non-invasive biomarker.

Methods

FACS-sorted peripheral immune cell RNA sequencing was performed on a small cohort (n=20) to profile the gene expression of major leukocytes in PCa and non-cancer groups, followed by qPCR validation on a larger cohort (n=73). In silicon deconvolution analysis was used to investigate proportions and expression profiles of the cell subtypes in our RNA-seq result and public datasets, together with FACS, immunofluorescence (IF), and qPCR on fresh blood samples collected from pre-biopsy patients in the hospital and healthy individuals.

Results

Four types of lymphocytes including $CD4^+$, $CD8^+$ T cells, NK cells and B cells were FACS-sorted for RNA-seq, among which the $CD8^+$ T cells, NK cells and B cells showed significant differences in gene expression profiles and demonstrated the ability to separate PCa and non-cancer cases. Focusing on $CD8^+$ T cells, we confirmed 6 differentially expressed genes at $p<0.001$ or false discovery rate <0.05 using qPCR analysis. Deconvolution analysis on the sorted bulk RNA-seq data estimated alterations in abundances and gene expression of the cell subtypes of these lymphocytes between cancer and non-cancer group. Subsequently, FACS and IF results confirmed such alterations in the proportions of the cell subtypes in circulation.

Conclusion

The results provide insights into the early peripheral immune response to PCa and suggest peripheral immune cells as a potential biomarker for non-invasive early PCa detection.