Establishment of a novel transcriptome analysis for metastatic castration-sensitive prostate cancer using long-read sequencing technologies

Takayuki Sumiyoshi[1], Arinobu Fukunaga[1], Maki Fujiwara[1], Kodai Hattahara[1], Kensuke Hikami[1], Kei Mizuno[1], Takayuki Goto[1], Akihiro Fujimoto[2], Shusuke Akamatsu[3], Takashi Kobayashi[1]

Affiliations:1. Department of Urology, Kyoto University Graduate School of Medicine, Kyoto, Japan, 2. Department of Human Genetics, The University of Tokyo, Graduate School of Medicine, Tokyo, Japan, 3. Department of Urology, Nagoya University Graduate School of Medicine, Aichi, Japan

Backgrounds: The treatment landscape of metastatic castration-sensitive prostate cancer (mCSPC) has recently become complicated, and rational biomarkers based on biological evidence might enable optimal treatment for each individual patient and improve treatment outcomes. We aimed to establish a transcriptome analysis of diagnostic prostate biopsy samples for mCSPC using long-read sequencing technologies.

Methods: Diagnostic prostate biopsy tissues and blood samples were being prospectively collected from treatment-naive de novo mCSPC patients at 22 university hospitals in Japan. Fresh tumor tissue specimens are halved and stored in RNA-stabilized reagents immediately after biopsy (within 30 seconds) to avoid degradation of nucleic acids. As a control, benign prostatic tissue samples were also collected from patients with benign prostatic hyperplasia. RNA samples with RNA Integrity Number (RIN) values >7 were selected and sequenced using the MinION sequencer (Oxford Nanopore). Sequencing data was analyzed using a pipeline named SPLICE. We explored differentially expressed genes (DEGs) and differentially expressed transcripts (DETs) associated with mCSPC biology by comparing tumor tissues and benign tissues.

Results: RNA was extracted from 104 tumor tissues, and 77% (80/104) met the quality control criteria for long-read transcriptome sequencing. After filtering low-quality reads, an average of 13 million reads was obtained with an average read length of 1,286 per tissue sample. Unsupervised clustering of transcripts demonstrated clear segregation of mCSPC tumor tissues versus benign prostatic hyperplasia tissues (**Figure 1**). Our analysis identified 1831 DEGs and 5140 DETs after adjusting for multiple testing (FDR < 0.01) (**Figure 2**). Among the genes with DETs, 1049 genes (1401 transcripts) were not detected as DEGs (DET-specific genes).

Conclusions: These data support the feasibility of transcriptome profiling of prostate biopsy tissues for de novo mCSPC using long-read sequencing technologies. Long-read transcriptome sequencing may provide a further understanding of mCSPC transcripts.

Funding Acknowledgements: This work was supported by a Prostate Cancer Foundation Young Investigator Awards (to Takayuki Sumiyoshi) and a Japanese Urological Association Science Award (to Takayuki Sumiyoshi).

Conflicts of Interest Disclosure Statement: All authors have no COI with regard to this study.

Figure 1

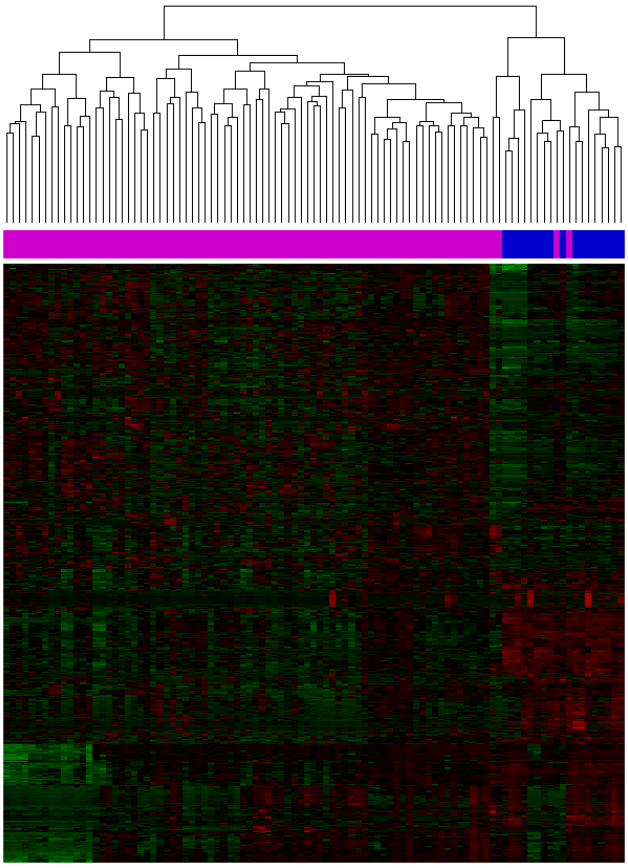

Figure 2