106P

106P Comparative analysis of urinary and tissue tumor DNA in muscle-invasive bladder cancer by boosted whole-exome sequencing

Jingyu Zang[1], Ruiyun Zhang[1], Feng Xie[2], Yue Zhang[2], Pan Du[2], Shidong Jia[2], Haige Chen[1], Guanglei Zhuang[1]
[1]Department of Urology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, [2]Huidu Shanghai Medical Sciences Ltd, Shanghai, China.

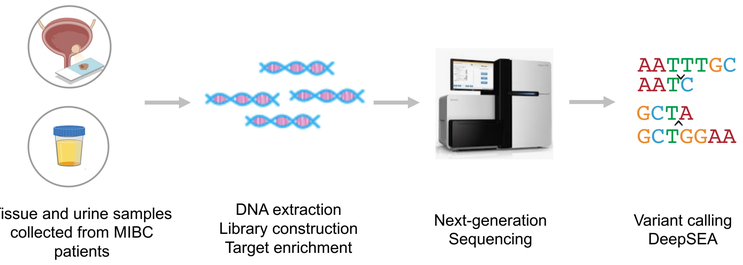
INTRODUCTION

Urinary tumor DNA profiling is promising for the diagnosis, monitoring, and treatment stratification of bladder cancer. However, previous studies mainly used the targeted next generation sequencing (NGS) panel approach, which is limited to predefined genes and thus lacks comprehensiveness. Here, we apply the boosted whole-exome sequencing (WES) to urinary and tissue tumor DNA in muscle-invasive bladder cancer (MIBC) to comprehensively compare the mutation profiles in matched urine and tissue samples.

METHODS

Matched tumor tissue, urine and peripheral blood mononuclear cells (PBMC) samples were collected from twenty MIBC patients. Nineteen tumor tissue, nineteen urine and twenty PBMC samples passed sample quality control were processed for NGS. PredicineWES+, an NGS assay with whole-exome coverage and boosted coverage in 600 cancer related genes from the PredicineATLAS panel, was applied to matched tumor, urine and PBMC samples for variant profiling. Mutation profiles of tumor tissue and urinary DNA were analyzed and compared.

Figure 1. PredicineWES+ NGS workflow



RESULTS

Figure 2. Mutation profiles of urinary and tissue tumor DNA from MIBC.
Mutation profiles of urinary and tissue tumor DNA were highly concordant across patients, with frequently mutated genes (*TERT, TP53, ARID1A, KMT2D, KDM6A, PIK3CA,* etc.) displaying comparable prevalence. Two tissue samples with sequencing QC failed were not shown.

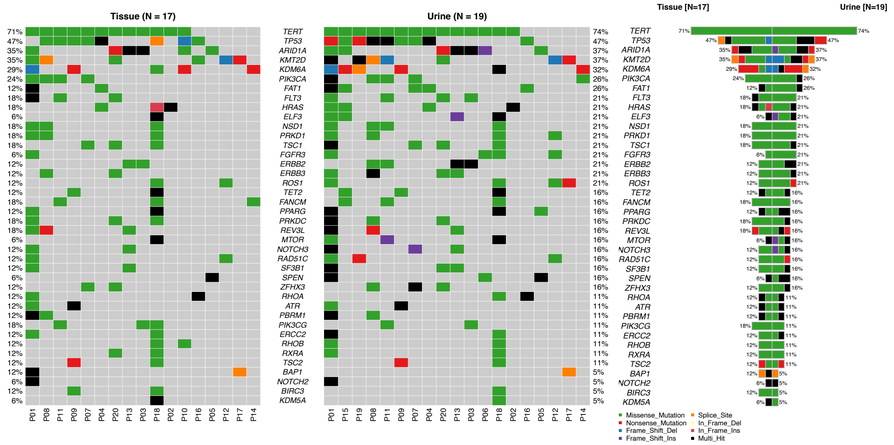


Figure3. Concordance of the mutations detected from the tissue tumor DNA (tDNA) and urinary tumor DNA (utDNA) by PredicineWES+. Number of mutations detected from the tDNA and utDNA in the WES regions (a, b) and ATLAS regions (c, d) were compared. Majority of the tDNA mutations (67.5% in WES regions and 80.1% in ATLAS regions) were also detected in utDNA. However, less than half of the utDNA mutations (42.1% in WES regions and 39.9% in ATALS regions) were detected in tDNA.

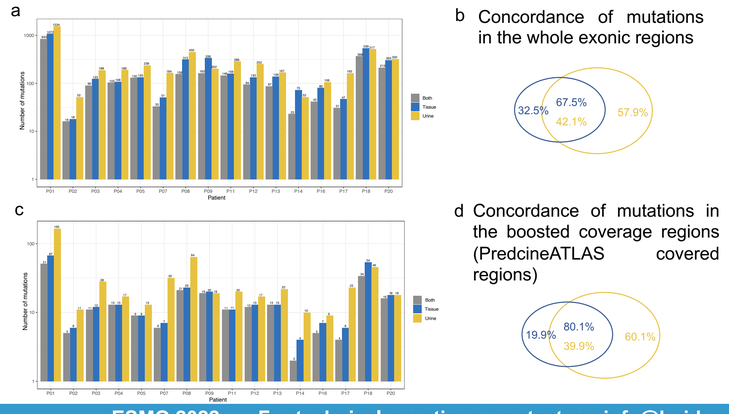


Figure 4. Tumor fractions inferred from tDNA and utDNA.
Tumor fractions (TFs) inferred from paired urine (2-52%) and tumor tissue (17-68%) showed significant difference (a, $p = 0.05$). Though TFs in urine were relatively lower, more somatic mutations were detected in urine than in tumor tissue (b, $p < 0.05$).

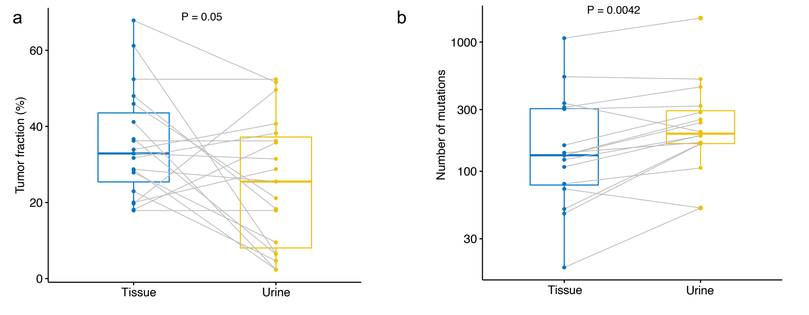
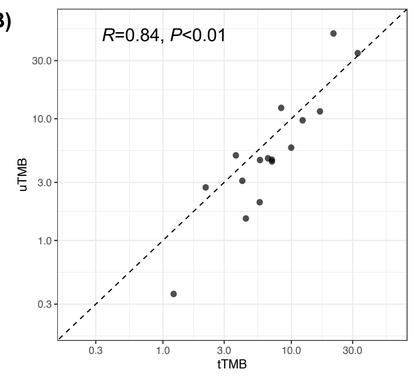


Figure 5. Tumor mutation burden (TMB) detected from tDNA and utDNA.
The TMBs detected from tDNA and utDNA were highly correlated (R=0.84, P<0.01).



CONCLUSIONS

This study demonstrates the effectiveness of urinary tumor DNA as a tissue surrogate for mutation profiling in MIBC at the whole-exome scale, supporting urine-based noninvasive molecular profiling in precision medicine for patients with bladder cancer.