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Molecular mechanism in prostate cancer with TP53 mutation

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Backgroud

The key roles of the TP53 mutation in cancer have been well established. However, the molecular mechanism differences of prostate cancer (PC) stratified by the TP53 mutation status has not yet been described.

Methods

Patients diagnosed with prostate cancer were enrolled in the study. Tumor tissue and matching blood were sequenced by next-generation sequencing (NGS) techniques with Acornmed panel with 808 cancer-related genes. Comprehensive molecular characterization was analyzed.

Results

A total of 599 patients with PC were enrolled including 90 patients with TP53 mutation (mut) and 509 patients with TP53 wild-type (wt). In TP53 mutation cohorts, the five most frequently mutated genes were TP53 (100%), BRD4 (19%), KMT2D (18%), ATRX (17%), and BRCA2 (15%). For TP53 wt cohorts, the five most frequently mutated genes were BRD4 (18%), AR (14%), FOXA1 (13%), CDK12 (12%), and BBC3 (11%). 88 frequently mutated genes were significant difference between TP53-mut and TP53-wt cohorts, such as KMT2D, ATRX, KMT2C, BRCA2 and PTEN, excluding the TP53 gene. There was no distinct signature between TP53-mut and TP53-wt cohorts. Signature 13 for APOBEC Cytidine Deaminase signatures, signature 5 for aging and signature 6 for defective DNA mismatch repair were only existed in TP53-mut cohorts, whereas signature 1 for spontaneous signature 3 for defects in DNA−DSB repair by HR were only discovered in TP53 wildtype cohorts. In the TP53 mutation cohorts, mutated genes were mainly enriched in the cancer pathway, PI3K-Akt signaling pathway, and Ras signaling pathway. However, in the TP53 wildtype cohorts, the primary pathways included the cancer pathway, PI3K-Akt signaling pathway, and Focal adhesion pathway.

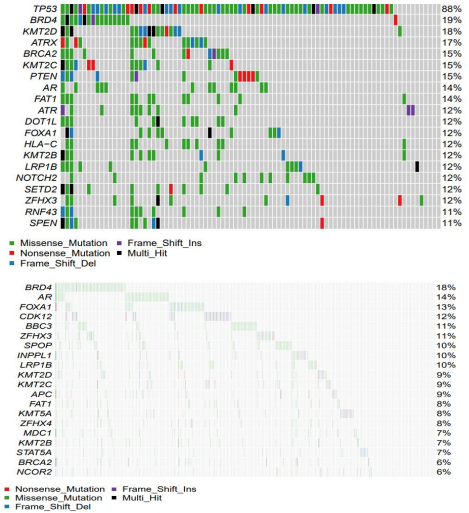

Figure 1. Landscapes of frequently mutated genes in patients with TP53 mutation and wildtype.

Conclusion

There were characterized the genomic differences and similarities, stratified by the TP53 status, which may reflect the PC patients with TP53 mutation harbored specific molecular mechanism.Patients with TP53 wt are more likely to benefit from immunotherapy, PARPI.

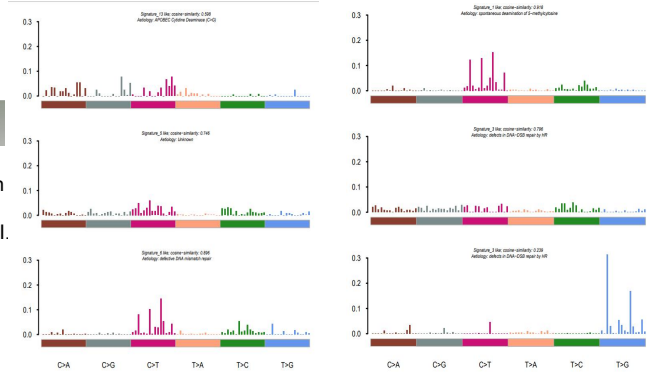

Figure 2. Mutational signatures for patients with TP53 wildtype.

Conflicts of Interest

The authors declare that they have no competing interests.

References

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